The New England
Journal of Medicine

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Volume 244 MAY 31, 1951 Number 22

ANNUAL ORATION

HOW SPECIALIZED IS A SPECIALTY?*

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BOSTON

MR. PRESIDENT, fellow-members of the Massachusetts Medical Society, ladies and gentlemen: Permit me, first of all, to thank you for the great honor you have done me by enrolling me among the pre-eminent members of the profession who have previously borne the title of orator. Indeed, I feel myself to be more than usually honored because, as it happens, my father, Dr. John C. Munro, received this same distinction forty-one years ago. It is not often that the son is given the opportunity to follow so exactly in the footsteps of a distinguished father.

According to Burrage's history of the Massachusetts Medical Society, the first oration was delivered in the year 1804 by Dr. Isaac Rand of Boston. He spoke on "Phthisis Pulmonalis, and the Use of the Warm Bath." During the following 147 years and 141 orations, the titles of only 3 have suggested that the author had any concern about specialization in medicine. The first was by Dr. Timothy Childs of Pittsfield and had the fighting title of "Rational Medicine — its Relations to Specialists, the Partisans of Exclusive Systems, and to Empirics." Forty-seven years later, in 1906, Dr. John L. Hildreth of Cambridge addressed the society on "The General Practitioner and the Specialist" and finally, thirty-four years after that, our beloved teacher, mentor and dean of neurosurgery, William Jason Mixter, spoke on "New England Neurosurgery and the Neurosurgeon." During this time orations were given by specialists, to be sure, — notably Dr. Harvey Cushing in my own field, — but none of their titles suggested any concern with the specialty *per se* or its impact on general medicine and surgery. Knowing nothing but my own branch of surgery, but having seen it, perhaps, more from the rough-and-tumble and general-practice aspect than most neurosurgeons of my time, I feel that a consideration of today's neurosurgery and its place in the practice of so-called general surgery in so far as the care of patients is concerned may be of interest. It is for this reason that I have chosen as my subject the title "How Specialized is a Specialty?"

Before exploring the details of this problem it will be well to reach, if possible, some conclusion about what constitutes a specialist and a specialty. It is easier to define a specialty than to define a specialist. A specialty is that branch of surgery or medicine that is practised by a specialist. Now, what is a specialist? Many are prepared to accept the somewhat disrespectful definition that states that a specialist is one who knows more and more about less and less. The exponents of this point of view, however, forget that if this be true the analogue that holds that a general surgeon is one who knows less and less about more and more must also be true. No general surgeon could be expected to take such a definition lying down. Despite their obvious deficiencies, however, these definitions are perhaps as near the truth as any others that can be devised.

We cannot define specialists and specialties by citing examples. For instance, an otolaryngologist must have more than a speaking knowledge of the skull and the function of parts of the brain — both within the field of neurosurgery and outside his specialty; the orthopedic surgeon claims peripheral nerves as his own and certainly deals extensively with broken backs and their contained spinal cords; the general surgeon has recently been doing things to the vagus nerves (to his sorrow, I believe), and practically anybody who can wield a knife considers himself competent to operate on the autonomic nervous system. Even the psychiatrist has entered the field of surgery by way of that common household implement, the ice-pick. Such intrusions of a specialist into fields other than his own, whether they be those of other specialties or in the general area, are common and well recognized. Neurologic surgery is no different from the others. For example, today's neurosurgeon must be able to recognize and deal with a tension pneumothorax, urinary obstruction, paralytic ileus and the contents of the triangles in the neck. Furthermore, all

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 22, 1951.

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physicians, no matter what else they may be proficient in, must be familiar with such subjects as modern fluid metabolism, chemotherapy, the use of antibiotics and blood transfusion, the treatment of shock and similar basic knowledge, which if pursued to its point of greatest proficiency will make a specialist out of every general man. Sir Robert Jones, who I suppose was one of the first really great specialists, says in the preface to "The Orthopedic Surgery of Injuries":

> The contributions of this volume will help to prove how necessary it is that a thorough knowledge of general surgery should be possessed by any surgeon who practices a special branch. Nothing is more fatal to progress than when, from defect of general surgical training, a specialist is limited to one view of a subject.

This was in 1921. That statement is as true today as it was thirty years ago. It needs modification, however, to the extent that as the specialist becomes more specialized so does his need for a generalized working knowledge increase well beyond the fundamental preparatory education he has received along such lines.

Can we define specialism by a consideration of its antithesis? The practice of general surgery prior to 1910 included more than a working knowledge of the practice of most specialties. My father could not by any stretch of the imagination be classed as other than a general surgeon. His pet love was gastric surgery, but I am told by those who worked with him that he was a master anatomist, as indeed he should have been, considering the years he prosected and taught under Dr. Thomas Dwight. Perhaps it was for this reason that his writing included neurosurgical papers on pachymeningitis hemorrhagica, trephining for epilepsy and laminectomy for cord injury and others on infections, including actinomycosis and typhoid perforation, on all varieties of abdominal surgery, on genitourinary and chest surgery, on fractures, on intussusception and a method for closing the patent ductus arteriosus in the newborn, on aneurysmorrhaphy for abdominal aneurysm and others. This wide diversity of interest and accomplishment differed in no way from the activities of other surgeons of his generation and is instanced to demonstrate what constituted the field of a true general surgeon. Something approaching this kind of general surgery is still practiced outside the large municipal and teaching centers. The general surgeons who do such practice, however, have come to depend more and more on these centers for help but nevertheless are obliged to practice many specialties in a general way. From this attempt at a definition we can but learn again that the measure of proficiency of any specialist is his basic knowledge of generalities.

So far as an individual specialty goes, it must be conceded that neurologic surgery is commonly considered a specialty among specialties. This conception was justified up to the close of the first world war, but since that time this special field has continually widened its boundaries. Today neurosurgery is no longer what it used to be — the surgery of brain tumors, with a few forays into the treatment of pain. The case load has shifted, and now the bulk of neurologic surgery is concerned with the treatment of injuries to the nervous system. Tumor surgery has been relegated to a secondary role. For example, over the past 21 years there have been 10,243 admissions to the 30-bed neurosurgical service at the Boston City Hospital. This series may be considered typical of the neurosurgical case load in any given community, except that it has been concentrated in point of view of time and the injury group is weighted with patients whose condition either was serious or required operative therapy. Fifty-six per cent or over 5700 of these patients suffered from injuries to the nervous system. Large as this figure is, it errs on the side of conservatism, since it does not include the great number of relatively minor craniocerebral injuries that are treated at home by a general surgeon or else never reach the doctor. In comparison only 14 per cent or 1400-odd patients of the 10,000 had tumors. This figure is probably weighted in the opposite direction because of the close association of the neurosurgical with an active neurologic service. Other similar figures are obtainable from the 1949 report of the National Safety Council as quoted by Mock, but this personal experience is perhaps enough to emphasize my point.

The care of such injuries calls for a high degree of truly general surgical knowledge. Of course, the judgment that is necessary in the treatment of any surgical emergency is a fundamental requirement. In addition, such effective and modern treatment as is required in spinal-cord injuries, for example, necessitates a knowledge of orthopedics, of proper understanding and care of the genitourinary tract, of dietetics, of plastic surgery and of modern physiotherapy and its offspring, ambulation training. Who can deny that this specialty has broadened to a point where it is rapidly approaching the status of general surgery in so far as the needed working knowledge of the specialist is concerned?

This broadening of the scope and shift of the case load to the field of trauma, of what used to be the surgery of brain tumors, poses far-reaching questions that must be answered by the general surgeon and specialist alike if the patient is to get his due. By their very nature the majority of these injured members of the public first apply for their treatment to the general surgeon. He sees them in a local hospital, which has neither a neurosurgeon on its staff nor a neurosurgical service as part of the hospital set-up. He, a general surgeon, has to be equipped to deal with a specialized problem. That this is not a figment of the imagination is instanced

by another study by Mock.* This has to do with the classification of doctors who cared for 7700 patients with craniocerebral injuries. In 65 per cent of the cases no neurosurgeon was available at all and of the remaining 35 per cent a part were seen only in consultation by a neurosurgeon. Thus two thirds of this group of cases, which was made up of head injuries and nothing else, were cared for by the general surgeon.

Is this practical need on the part of the general surgeon for specialized training met by our medical schools? Do they train their undergraduates to deal adequately with this load, which as graduates they may have to shoulder in spite of themselves? The answer is no. Through the kindness of the dean's office of the Harvard Medical School I have been enabled to review the announcements of courses sent out by 85 Class A medical schools in the United States and Canada. Forty, or virtually one half, make no announcement relative to the teaching of neurologic surgery. As far as the relation of these schools to their students goes, neurosurgery is not worth talking about. Thirty-two others have a subdepartment of neurosurgery, usually headed by a professor of clinical surgery with "Neuro" in parenthesis after his title or by a clinical, associate or assistant professor of neurologic surgery. This is strictly camouflage, however, because these appointments are under the control of the department of surgery. The appointees have no autonomy of their own and are granted as few teaching sessions as it is possible to give them. For example, in one large school all formal neurosurgical teaching occurs in the third year. Of the assigned five hours, one covers all trauma to the nervous system, two, intracranial surgery — presumably technic, — one, the peripheral nerves and one the autonomic nervous system. Aside from the obvious practical futility of these assignments, it is apparent that in this school, at least, injuries to the nervous system and their treatment are not regarded as being particularly important. This point of view would doubtless change should the professor's child be rendered unnecessarily decerebrate or paraplegic because of lack of knowledge on the part of the graduate who had to care for it after an automobile accident. Only 13 schools have separate departments of neurologic surgery. Thus only 15 per cent of the Class A medical schools in the United States and Canada make anything like an adequate attempt to provide an educational background for the care of injuries to the nervous system. The reasons for this are all too plain. In some, at least, of these schools the department of neurosurgery is extant because of a special endowment, and it is a question of either having a department and the use of the money that goes with it or not having the money. This is a compelling reason for the pursuit of higher education. In all schools the problem of available time in relation to the number and relative importance of the subjects to be taught is critical and demands a practical solution. Something, indeed many things, have to go by the board, and what is more suitable for relegation to the postgraduate level than the surgery of brain tumors, even if that relegation does happen to take the surgery of brain injuries with it? I can offer you no solution for this difficulty other than the one that is fundamental to all medical teaching. This is the basic tenet that all good doctors want to know as much as they can about the conditions they are called on to treat and if they do not get appropriate basic knowledge in the medical schools they will acquire it in some other way. At present education in neurologic surgery, — and especially in the traumatic variety, — must be on a postgraduate level and must be initiated by the individual practicing physician.

Are the communities, as represented by their hospital trustees and other personnel, alive to the implications of this generalization of a specialty? Again, the answer is no. Consider for a moment the plight of the citizen who has been rendered paraplegic or quadriplegic as the result of a spinal-cord injury. He is taken to his community hospital and receives his first treatment from a general surgeon. With rare exceptions, and in spite of the tremendous advances that have been made in the past ten years in the rehabilitation of such patients, the general attitude of the doctor, the family and friends is that the sooner this patient dies the better. There is lacking, therefore, a proper driving enthusiasm for his treatment. Bed sores, kidney and bladder stones, spasms, deformities, perpetual bed care with long hospitalization, special nursing and attendants are all regarded as inevitable accompaniments of his injury. Soon, if they have existed at all, the financial resources run out. To the pressure that has been exerted by the staff on the doctor-in-charge to empty this bed for more fluid, more operable and better-paying patients is added even greater pressure by the superintendent to get rid of this unremunerative burden on his hospital resources. The victim, therefore, shortly finds himself transported to the county hospital or the medical poorhouse. Here he soon learns that he can look forward to nothing better than to put an end to his own misery and the financial and emotional drain on his family by an early death. Even if the supply of money is unlimited the outlook for rehabilitation that *should* be provided for him is discouraging to a degree. Outside of a few veterans' and armed-services hospitals one can count on the fingers of one hand the civilian or community institutions that are equipped to care properly for such a patient.

Aside from the obvious uncharitableness, is it good business for any community to neglect its citizens in this manner? The Liberty Mutual In-

*Mock, H. E. *Skull Fractures and Brain Injuries*. 806 pp. Baltimore: Williams and Wilkins, 1950.

surance Company, under the guidance of one of its vice-presidents, Mr. Stanwood L. Hanson, has demonstrated that in so far as industrial injuries are concerned, it is not. Their conclusions are equally applicable to the communities and the non-industrially injured. Because in this and 34 other state and Federal jurisdictions paraplegic and quadriplegic patients under the Workmen's Compensation law are considered to be permanently and totally disabled, medical services including hospitalization, nursing and attendant care as well as medical supervision and therapy must, if necessary, be rendered to such a patient throughout his life. In 21 of the same jurisdictions indemnity payments must also be made to such patients for the same period. To meet these possible expenses it has been the custom of the company to estimate and earmark for future costs the amount of money necessary to meet these legal requirements. These estimates have been based on life expectancy, surgical complications and so forth. Rehabilitation has not entered the picture. Such estimates have been known to exceed $100,000 per patient for medical costs alone and to have reached the astonishing amount of $400,000 in a patient with quadriplegia. In the face of such figures, and because they were getting relatively no return on their investment, the company undertook to provide modern rehabilitation for fourteen paraplegics and quadriplegics. Their intention and expectation was to reduce or eliminate the expense of hospital, attendant and medical care by teaching the patients to lead self-reliant, healthy lives at home. No saving was attempted in the indemnity payments. Any re-employment that might eventuate was regarded as an unexpected bonus. Without such a program of rehabilitation they estimated that their costs for these fourteen patients would be $1,127,700. With the patients treated according to the best medical and hospital standards for the care of those paralyzed as the result of a spinal-cord injury, the rehabilitation as outlined above of these 14 paralytics actually cost $115,830. The company's estimated savings, including medical and indemnity payments, was $903,900. In addition, all patients, besides being free of the need for hospitalization, free of the need for attendant care, able to live at home and needing no more medical care than a periodic six months' examination, have returned to some form of sedentary work or are engaged in their own businesses. These range from repairing watches to driving a truck with special controls and conducting a trucking business. It is all too obvious that if one can save one million dollars by spending one hundred sixteen thousand the effort and investment is well worth making, even for a community, and even if it takes the form of providing more beds in institutions where the ability and the will to carry out rehabilitation are present.

The need for rehabilitation is not peculiar to spinal-cord injuries alone. It is necessary in some form in all patients who are suffering from an injury to their nervous system. It necessitates active interest and co-operation on the part of the staff and the trustees of the hospitals that have the responsibility for the care and welfare of these injured. Meeting this responsibility is not difficult, though the need to do so is by no means universally recognized, — particularly not by the larger municipal and some teaching hospitals. No such hospital can be considered complete, modern or equipped to render the service that is expected of it if it does not have a formal neurosurgical department with a specially trained visiting and house staff. The plea that there is not enough neurosurgery to justify the expense of such a specialized service in the communities that support such a hospital can no longer be sustained in the light of the generalization of this specialty. This is particularly true since these hospitals must act, in addition, as centers of information, teaching, consultation and reference for the smaller hospitals in the smaller communities. They must be prepared to accept in transfer all serious, undiagnosed, difficult, deteriorating and operable neurosurgical problems. It is on them that the burden of rehabilitation falls most heavily, and that they don't like it is no reason for not accepting it. They cannot avoid their responsibilities and keep faith with the public. Moreover, they set the standard and are responsible for the kind of neurosurgery that is done within the circle of their influence. Save for rare exceptions, proper neurosurgery can and should only be done with the equipment and by the staff of a neurosurgical unit in a large general hospital. That done in small community hospitals by specialists who travel over the country operating in one hospital after another is bad neurosurgery. It is bad for the local doctor because he has to accept more of the responsibility for preoperative diagnosis and preparation and for postoperative care than he is able or trained or should be expected to. It is bad for the peripatetic consultant because it is a deliberate performance that is contrary to all his training and is a sacrifice of his ideals and an affront to his knowledge of what is best for the patient. It is bad for the patient because it deprives him of his proper right to survival and complete recovery without affording him any opportunity to object to this deprivation. It is better for the patient to spend his time traveling to a place where he can be properly treated in the most skilled manner than to waste it staying in a place where the treatment is bound to be inadequate no matter how skillful the operative technic.

There is only one exception to this, and that is associated with the impossibility of moving a neurosurgical patient because of the breakdown of public and private transportation. If, in such circumstances, the patient's life can only be saved by

an emergency neurosurgical operation done in the local hospital, then some local surgeon trained in the fundamentals of traumatic neurosurgery must assume the responsibility and shoulder the burden of operating. He will be faced with only a few operative choices, however; a subtemporal decompression, usually with the removal of either an extradural or a subdural clot and the possible closure of the middle meningeal artery, possible débridement of a compound fracture or bullet wound of the skull and a diagnostic stab wound and therapeutic section of the tentorium and incisura tentorii are the cranial ones, whereas a decompressive laminectomy and possible débridement of a compound fracture, gunshot or stab wound of the spine are the spinal ones. The necessity for meeting such an emergency predicates an adequate minimum of equipment kept ready for use at all times in all small hospitals. This is the primary responsibility of the trustees. It also predicates the education of at least one and possibly two members of the surgical staff in basic neurosurgical nonoperative therapy and operative technic, particularly as they apply to trauma. This is the primary responsibility of the staff but is also inescapable on the part of the trustees. The specialized use of this knowledge in so far as actual operating goes will and should be very infrequent but — and this is a big "but" — these specially trained general surgeons should be the men who will direct the first treatment of all such injuries; who will have the responsibility for seeing and will see that the serious, the undiagnosed, the difficult, the deteriorating and the operable patients are transferred at once out of their hospitals to the large municipal centers that are properly equipped to care for them; and who will be responsible for the immediate care and eventual rehabilitation of those patients who can be treated locally. They are the surgeons who keep down the mortality and morbidity of those injured patients.

I have still defined neither a specialty nor a specialist, but I hope I have indicated that at least one specialty — and one that by tradition has been strongly delimited — has a general surgical aspect. Because of this I urge and believe that the general surgeon who has to practice all kinds of surgical specialties under the hardships imposed on him through the necessary use of small community hospitals must equip himself with a fundamental knowledge of traumatic neurosurgical therapy. Only in this way will he be able to separate those patients that he can from those that he cannot treat. To help to meet this extra load the large centers on their part should have beds and personnel competent to receive his difficult cases, should provide him with opportunities for postgraduate studies along lines that will be practical and useful to him, should set proper standards for the practice of neurosurgery and guard him against the depredations of the peripatetic specialist and aid him to an increased efficiency and a truer appreciation of his own influence and importance in the community.

How specialized *is* a specialty? I don't know, but I strongly suspect that all *surgical specialties* are actually much more general then they are usually considered to be. I am sure that this is true of neurosurgery. Perhaps, therefore, we should revise our thoughts and our teaching, recognize that the pendulum has swung too far and make some effort to get back toward but not to the standards of forty years ago. Surely, with our technical know-how and what we have inherited of our fathers' brains and willingness to work, we can expect to lift both general and specialized surgery to even greater heights than they have already attained.

TREATMENT OF EOSINOPHILIC PNEUMONOPATHY*

Report of a Case Treated with ACTH

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THE authors have recently treated an unusual case, which was characterized by a high blood eosinophilia and an increasing pulmonary infiltration. The patient's disease has been difficult to classify. She was much more acutely ill than the average patient with a Loeffler syndrome. Apley and Grant,[1] in 1945, discussed the possible relation of some of the conditions of eosinophilia and pulmonary infiltration and termed them the "E–P syndrome." The patient fits into this general category. She was eventually treated with adrenocorticotrophic hormone (ACTH), which appeared to be life-saving for her.

CASE REPORT

Prior to the time of hospitalization, the patient, a 41-year-old housewife, had been relatively healthy, except that she became clinically allergic at the age of 15 and developed hay fever. At that time she noted allergic symptoms on contact with roses. After this she became generally allergic the year around and had intermittent nasal discharge, lacrimation and a nonproductive cough. In the past, allergic surveys by other physicians had revealed very little. In January, 1947, she developed asthma characterized by wheezing, asthmatic rales and considerable coughing. It continued intermittently until September, 1948, when it suddenly disappeared. During this time a routine chest film was made. It was interpreted as negative. After a severe cold in December, the asthma returned but shortly disappeared. In March, 1949, she had a mild cold and again noted wheezing respirations. She felt better on recovery from the cold.

In July, 1949, the patient made a motor trip to California by way of New Mexico and Arizona. On her return to Denver on August 1, she was exhausted. The patient is a conscientious mother and works hard. On this trip her three children were ill with respiratory infections almost constantly. The patient noted no dust storms either en route to or returning from California. About August 4, 1949, she again developed symptoms of a cold, with a cough. She placed the onset of her severe illness at this date. She became progressively weaker, had a nonproductive cough and developed moderate dyspnea. She was hospitalized on August 20, 1949. The temperature was slightly elevated (100.4°F.) and the pulse 90. A chest roentgenogram revealed pulmonary infiltration of the left apex (Fig 1*A*). Examination of the blood revealed a sedimentation rate of 103 mm. in 1 hour and moderate secondary anemia, with a hemoglobin of 11.5 gm. and a red-cell count of 3,510,000. The white-cell count was 5050, with a differential of 60 per cent neutrophils and 40 per cent lymphocytes. The presumptive diagnosis was bronchopneumonia. Penicillin therapy was started on hospital entry, but after negative sputum and laboratory studies were returned the diagnosis of virus pneumonia was entertained and aureomycin therapy was begun. This was discontinued after three days because the patient tolerated it poorly. Streptomycin and penicillin were then instituted, without improvement. Ten days after admission, a second blood count revealed the same type of anemia, but at this time an eosinophilia of 14 per cent was noted. Because of her failure to improve, the patient refused to remain in the hospital and returned to her home on September 11. This decision was made despite the fact that a chest x-ray film taken at the time of dismissal showed an increase in the amount of infiltration in the left lung. A film taken ten days later showed essentially the same findings (Fig. 1*B*).

After a stormy course at home, she re-entered the hospital on September 24, with a low-grade temperature and rapid pulse rate. There were numerous moist rales over the entire left lung and coarse rhonchi on the right. A roentgenogram of the chest now showed extensive involvement of the right lung as well as of the left. Antibiotic therapy was again given. Repeated sputum studies were negative for acid-fast bacilli on smear and culture as well as for fungi and aerobic and anaerobic pathogenic bacteria. It was noted on many occasions that the sputum was loaded with eosinophils.

During this second hospitalization, when antibiotics such as aureomycin and Chloromycetin, as well as sulfonamides, gave no improvement, a diagnosis of either a Loeffler type of pneumonia or periarteritis nodosa was considered. Dr. John R. Mote of Armour Laboratories was consulted and agreed to supply ACTH for treatment of the patient. On October 7, balance studies for sodium, potassium and chlorides were started. During the previous week the patient had gone downhill rapidly. It was necessary to confine her to an oxygen tent. Her blood pressure was 104/58 and the pulse was 124 with an occasional irregularity. Her respirations were definitely labored, being 40 per minute. There was accentuation of the second pulmonic sound. No cardiac murmurs were heard. Loud, moist, crackling rales were present in both lung bases and scattered throughout both lung fields. Dullness was present over the left upper lung field and over the right base. There was no evidence of edema in the extremities nor in the sacral region.

Examination of the blood revealed an erythrocyte count of 3,810,000, a hemoglobin of 11.1 gm. and 12,400 leukocytes with a differential of 9 per cent lymphocytes and 91 per cent leukocytes, of which 35 were filamentous, 1 was nonfilamentous, 54 were eosinophils and 1 was a basophil. The absolute eosinophil count was 9100 per cubic millimeter. The urinalysis was negative. The sedimentation rate was 104 mm. in 1 hour. A chest roentgenogram showed marked bilateral pulmonary involvement (Fig. 1*C*).

ACTH was started on October 10, 25 mg. being given every six hours. Within twenty-four hours considerable improvement had occurred. The temperature dropped to normal. The blood sedimentation rate began to decline. After two days of therapy the absolute eosinophil count was 25 per cubic millimeter. A summary of the patient's hospital course is indicated in Figure 2. It will be noted that 50 mg. of ACTH was given the first day and 100 mg. daily for the next six days. Because of the tendency toward low urinary output, one dose of 25 mg. was omitted; this was shortly followed by a marked diuresis. The amount was progressively reduced as indicated, with the occasional omission of a six-hour dose, until finally the patient was receiving 10 mg. of ACTH every six hours. After this she remained in the hospital for a short time and then was dismissed. She was maintained on diminishing doses of ACTH for a few more days at home. After the second day of ACTH therapy, it was no longer necessary to continue with the oxygen tent. The chest roentgenograms show the remarkable response to this therapy (Fig. 1*D* and 1*E*).

The sodium intake was kept at a relatively low level. With the administration of ACTH the urinary sodium output dropped immediately; this continued until the amount of ACTH was reduced. In conjunction with the low sodium output, the patient's weight showed a steady increase, going from 122 to approximately 130 pounds. The weight later diminished when the dose of ACTH was reduced, and the

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sodium output again took place. Studies of the potassium intake and output, the former being maintained at a high level, showed almost no change. Other investigators[3] have reported that with the administration of ACTH the potassium output may or may not increase.

The patient was allowed to return to her home on October 26 and was advised to remain in bed. At first she continued to improve, but she gradually developed a moderate unproductive cough. There was a tendency for the blood eosinophilia to return, and on November 1 it was noted as 11 per cent, with a sedimentation rate of 55 mm. in 1 hour. A roentgenogram of the chest showed a questionable recurrence of the infiltration. On November 9 a definite infiltration in the left lung was again noted, and the eosinophilia tended to recur. The count persisted at about 12 per cent for a number of months. On October 4, 1950, the eosinophil count was 6 per cent and the white-cell count 8000. All roentgenograms, including the last one, taken in October, 1950, were normal.

Discussion

Eosinophilia and pulmonary lesions are commonly associated in bronchial asthma, Loeffler's syndrome, tropical eosinophilia, certain intestinal infestations, periarteritis nodosa and eosinophilic leukemia. Wintrobe[3] has listed nine causes of eosinophilia

Figure 1*A*. *Roentgenogram of the Chest Taken on August 20, 1949, Showing Infiltration of the Left Apex.*

Figure 1*B*. *Film of the Chest Taken Ten Days after Discharge on First Admission.*

Figure 1*C*. *Film of the Chest Taken on Second Admission before Beginning of ACTH Therapy.*

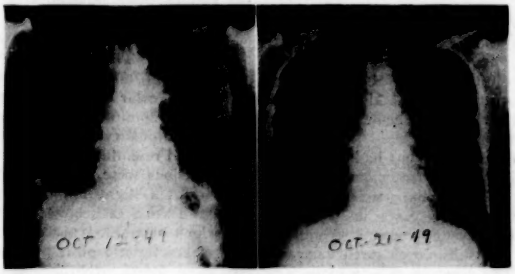

Figure 1*D*. *Roentgenogram of the Chest after ACTH Therapy.*

Figure 1*E*. *Roentgenogram of the Chest, Showing Further Improvement.*

was 18 per cent. Because of this she was hospitalized on November 15 for a second course of ACTH therapy. Smaller doses of the drug were given. Again the eosinophilia dropped, this time from 16 per cent to 1 per cent. The roentgenogram of the chest cleared markedly. She was dismissed from the hospital on the twelfth day. She had been given a total of 2.1 gm. of ACTH during both hospitalizations. Since that time she has remained relatively well and has resumed normal activity. She had one severe attack of urticaria, which appeared to be relieved with antihistaminic drugs. A recent complete allergy survey made in May, 1950, revealed only a moderate reaction to grasses and house dust. During the spring and summer of 1950, she had considerable hay fever, with a few mild attacks of asthma. The eosinophilia has

in the blood without reference to lung changes. Investigators[4, 5] have reported infiltrations in the chest in association with various parasites such as *Endameba histolytica*, larvae of *Ascaris lumbricoides*, trichinae, and nematodes of cutaneous helminthiasis. With these an eosinophilia usually occurs. In the present case the stools were checked for parasitic infestations; none were found.

A bone-marrow study was made. No disturbance of the hemopoietic system was revealed, other than

an increase in the eosinophilic myelocytes. In consideration of a possible familial anomaly other members of the family were checked; no tendency toward a high blood eosinophilia was found.

Periarteritis nodosa was carefully considered. A high blood eosinophilia can occur in periarteritis nodosa, as can asthmatic symptoms. Moreover, transitory pulmonary infiltrations have been noted radiologically. An attempt was made to obtain a biopsy of muscle of the patient, but permission for this was refused. Actually, no localized persistent muscle tenderness was noted. The marked pulmonary involvement in the absence of demonstrable disease of other organs, such as the kidneys, vascular system or nervous system seemed largely to rule out periarteritis nodosa.

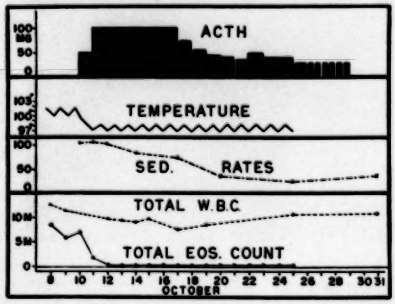

FIGURE 2. *Data on Course in Hospital on Second Admission.*

Despite the fact that this patient had never been in the tropics, a diagnosis of tropical eosinophilia was entertained. In Weingarten's[6] article on tropical eosinophilia, he reported 81 cases in which he found that expiratory dyspnea was a prominent symptom and that the spleen was often enlarged. All these patients had been in the tropics. The present patient had no enlargement of the spleen. In tropical eosinophilia, the patient usually presents a marked increase in the eosinophilic count at the onset of the disease, rather than in the third or fourth week, as occurs in the various allergic disorders. The clinical picture differs from that of tropical eosinophilia, in which there is an acute febrile onset. The fever lasts a few weeks and then becomes chronic. In this case the reverse was true, in that the onset was gradual, with slowly increasing severity. Herbert, de Vries and Rose[7] report a case of tropical eosinophilia that did not respond to ACTH therapy, either clinically or by a lowered eosinophil count. The case under discussion responded in both these ways.

Loeffler's syndrome is characterized by changing, even transitory, pulmonary infiltrations, eosinophilia of the blood and sputum and a relatively mild clinical course. Frequent x-ray examinations are necessary for diagnosis. Faison,[8] in 1947, in an excellent article on Loeffler's syndrome, reviewed the literature and discussed the pathogenesis of the condition. He emphasized that the pulmonary infiltrations are transitory and are usually out of proportion to the mild clinical course of the disease. He believed that the pulmonary infiltrations represent atelectases. If this is true, Loeffler's syndrome may be a variant of bronchial asthma in which the patient has an eosinophilia of the blood and especially tenacious bronchial secretion that tends to produce atelectasis. A similar clinical and roentgenographic picture is often produced by virus pneumonia — but without the presence of a marked blood eosinophilia.

Bayley, Lindberg and Baggenstoss,[9] in 1945, reported an interesting case of Loeffler's syndrome in which they described the pathological examination of the lungs and reviewed the pathologic changes in the lungs of other cases reported up to that time. Their patient presented ill-defined roentgenographic changes in the lungs and had shown mild asthmatic symptoms for seven years. She then developed moderately acute symptoms of fever, cough, dyspnea and eosinophilia, with marked pulmonary infiltrations. She gradually improved over a period of two to three months after sodium iodide was given intravenously. Then no report was received until three months later, when she rapidly became ill and died. The pathological examination of the lungs showed an advanced organization of a widespread alveolar and bronchial exudate, with a cellular predominance of eosinophils and a scattered granulomatous type of inflammation that had a superficial resemblance to tubercle formation. Vascular lesions were seen that showed thickening of the walls, a slight round-cell perivascular infiltration and areas of necrosis of the vascular wall, all of which resembled periarteritis nodosa but were not characteristic of it. Bronchial lesions similar to those found in bronchial asthma were noted. Our patient's pulmonary roentgenographic changes were progressive, widespread and fairly persistent. Her sputum contained numerous eosinophils. Until ACTH was administered she somewhat resembled Bayley's patient, both clinically and in the severity of her disease. The other autopsied cases classified as Loeffler's syndrome and cited by Bayley presented many of the lesions found in his case. In some of the cases the pneumonic exudate was not organized and the cellular portion consisted largely of eosinophils.

Pulmonary infiltrations associated with eosinophilia have recently attracted much clinical interest. In tropical eosinophilia there may be a question whether or not the disease is caused by

some infectious agent. Rich[10] has advanced the hypothesis that the lesions of periarteritis nodosa are the result of hypersensitivity. In 1942 he reported five autopsies on patients who had had serum sickness before death. In all of them he demonstrated the characteristic lesions of periarteritis nodosa. He later demonstrated[11] similar vascular lesions in one patient following a reaction to sulfonamide therapy, and in the next year Rich and Gregory[12] succeeded in producing similar lesions experimentally in rabbits by sensitizing them to horse serum.

Knowledge of the etiology of "E-P" syndromes (eosinophilic pneumonopathy) has gradually increased, although it is still far from complete. Human hypersensitivity,[13, 14] with its manifestations of anaphylaxis, allergy, alterations of the autonomic nervous system and glandular dysfunction, seems to play the major role. It is interesting to speculate on the effect of the apparent exhaustion of our patient's physical resources with the development of her severe "E-P" syndrome. Her adrenal glands responded rapidly and with vigor to the administration of ACTH. This indicates that if there were any pituitary-adrenal dysfunction it would involve the pituitary body with its nervous connections. Although she still exhibits evidence of hypersensitivity, her clinical condition is much as it was before July, 1949. After two courses of ACTH, the lung fields, as seen in roentgenograms, have remained clear for about a year. Others[8, 9] have reported seriously ill patients with the "E-P" syndrome who had long remissions. Some of those who were ill died before the advent of ACTH and cortisone. Our patient has been strongly urged to conserve her physical and nervous resources. The breakdown of these resources, with the possible addition of a respiratory infection, appears to provide the major clue to the causation of her illness — with due regard to her allergic background.

With the introduction of ACTH and cortisone and by virtue of their marked effect on the allergic phenomenon, a new method of treatment has become available. Thorn and his group[15, 16] reported that the injection of ACTH produced a marked drop in the number of circulating eosinophils. Following the work of Hench and his collaborators[17] with cortisone and ACTH, it was noted that there appeared to be an actual lysis of eosinophils. Randolph and Rollins[18] reported the beneficial effect of ACTH administration in cases of severe asthma and other allergic states. A number of other investigators[19] likewise have treated the same allergic conditions and eosinophilic pneumonopathy with ACTH.

Summary

A case is presented with the clinical history, course and laboratory findings that are consistent with the "E-P" syndrome. A wide range of antibacterial therapy had no beneficial effect on this patient. It was only after the use of ACTH that a dramatic improvement followed. The patient is still under observation. She has been active for over a year, although mild allergic symptoms and a low-grade eosinophilia persist.

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COMPLICATIONS OF THE DIURETIC PHASE OF LOWER-NEPHRON NEPHROSIS*

Report of a Case Manifesting Tetany

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RESUMPTION of urine flow after a period of anuria in lower-nephron nephrosis indicates a return of tubular function, and a favorable outcome may usually be expected. During the days when urinary output is greater than normal, however, renal function may still be abnormal and the condition of the patient precarious. It is the purpose of this paper to direct attention to certain complications that may be encountered after renal tubular function has been resumed, during the period when urinary output is massive.

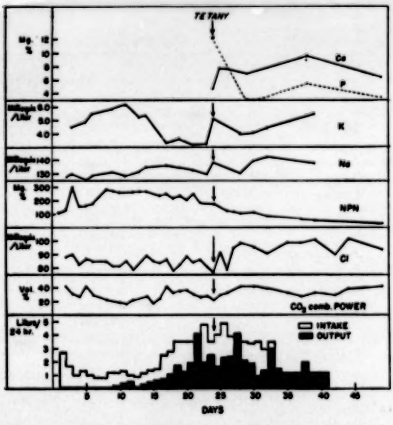

FIGURE 1. *Fluid Balance and Serum Electrolyte Changes in a Case of Lower-Nephron Nephrosis.*

The following case illustrates a number of problems associated with the diuretic phase of lower-nephron nephrosis. Tetany has not previously been reported in this condition.

CASE REPORT

K. O. (1357882), a 36-year-old woman, was admitted to the Gynecological Service of Boston City Hospital on April 24, 1950, because of vaginal bleeding of three days' duration and was transferred to the Fifth (Boston University) Medical Service after twelve hours of known anuria. Three weeks before admission, because of amenorrhea for one month and the likelihood of pregnancy, a self-induced abortion was attempted by means of the ingestion of Humphries No. 11 pills (a mixture of innocuous herbs) and Lysol douches (once daily, one teaspoonful per quart of water). Two weeks prior to entry the patient manipulated a catheter vaginally and noted within three days the appearance of a profuse foul black vaginal discharge, accompanied by crampy abdominal pains, chills and fever. Urinary output was allegedly ample until the day of admission. Past and family histories were not remarkable.

Physical examination revealed an acutely ill, dehydrated patient, who complained of nausea, vomiting and abdominal pain. Temperature, pulse, respirations and blood pressure were within normal limits. There was tenderness with spasm in both lower-abdominal quadrants and tenderness of the cervix and vaults. The cervix was soft, and there was a thick yellow-brown vaginal discharge.

Laboratory examination on admission revealed a nonprotein nitrogen of 103 mg. per 100 cc., a carbon-dioxide combining power of 40 vol. per 100 cc., a chloride concentration of 88 milliequiv. per liter and a hemoglobin of 6.9 gm. The hematocrit was 12 per cent and the white-cell count 17,600 per cubic millimeter, with a normal differential. Cultures of the cervix later revealed *E. coli*; blood cultures were negative. A small amount of urine obtained by catheter revealed ++ albumin and many red and white blood cells per high-power field.

When the correction of dehydration failed to produce an increase in urinary output it was thought that the diagnosis was septic induced abortion complicated by either lower-nephron nephrosis or renal cortical necrosis. Because of severe vomiting, the patient was maintained on parenteral fluids, which were continued for twenty-three days. A 12 per cent solution of glucose, to supply calories and water, and normal saline solution in sufficient amounts to maintain serum sodium and chlorides were administered on the basis of measured output of urine, stools and vomitus (plus 800 cc. for insensible water loss). Small amounts of packed red-blood cells were given because of anemia. Two gm. of calcium gluconate, 72 mg. of vitamin K and a soluble multiple-vitamin preparation were added daily to the intravenously given fluids. Penicillin in doses of 100,000 units was injected intramuscularly every four hours. Figure 1 illustrates the course of the significant laboratory determinations and fluid balance.

On the fifth day administration of digitalis was begun because of the appearance of sacral edema and basal pulmonary rales. It was continued for five days and then omitted because of improvement in these signs and because of evidence of excess digitalis effect on the electrocardiogram.

On the eleventh day Kussmaul breathing and mental confusion were noted. The carbon-dioxide combining power was found to be 18 vol. per 100 cc., and the serum potassium 6.2 milliequiv. per liter. An intravenous infusion of 250 cc. of a 4 per cent solution of sodium bicarbonate was given to combat the acidosis, and four rectal instillations of 50 gm. of acid resin were administered at six-hour intervals, in an attempt to adsorb potassium from the lower-intestinal contents. Within thirty-six hours, the serum potassium had dropped to 5.3 milliequiv. per liter, the carbon-dioxide combining power had risen to 29 vol. per 100 cc., and the patient appeared to be improved.

After thirteen days, during which the urinary output averaged 40 cc. per day, diuresis began, and by the twenty-second day the urinary output had reached 4150 cc. in twenty-four hours. On the twenty-third day, the serum potassium was 3.1 milliequiv. and the hemoglobin 6 gm.; an intravenous

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infusion of 4050 cc. of glucose in water and saline solution, 700 cc. of packed red blood cells and 8 gm. of potassium chloride was administered over a fourteen-hour period. Three hours after completion of the infusion the patient suddenly became dyspneic, orthopneic and cyanotic and began to cough up large amounts of frothy blood-tinged sputum. This episode of acute pulmonary edema was finally controlled by the administration of oxygen under positive pressure, rotating tourniquets, Demerol and digitoxin. A striking increase in heart size and an electrocardiographic pattern typical of left-ventricular enlargement were noted after the subsidence of the acute episode and persisted throughout the remainder of her hospital stay.

Some hours after the completion of the infusion described above, the patient complained of stiffness of the arms and legs. Twelve hours after the infusion had ended she suddenly became cyanotic, and a typical attack of tetany with severe carpopedal and laryngeal spasm occurred. A blood sample was drawn and 3 gm. of calcium chloride was administered intravenously over a five-minute period, with complete cessation of all signs and symptoms. An intravenous infusion containing 5 gm. of calcium chloride in 1000 cc. of a 5 per cent solution of dextrose in water was given during the next six hours. The pretreatment blood sample revealed a serum calcium of 4.8 mg., a phosphorus of 12.4 mg., a serum protein of 5.6 gm. (albumin 3 gm.) and a carbon-dioxide combining power of 22 vol. per 100 cc. Parathyroid hormone extract (Squibb) in a dose of 3 cc. (300 units) was administered every eight hours for two doses, and 100,000 units of vitamin D with 5 gm. of calcium lactate were given orally for the next five days. Digitalis was omitted during this period. There was no recurrence of symptoms. The serum calcium rose to 8.4 gm. and the phosphorus fell to 3.0 gm. After five days, with normal serum calcium and phosphorus values and with the patient on a high-calcium diet, all other calcium therapy was discontinued.

On the thirty-second day of her illness the patient became febrile. Urinary cultures demonstrated *A. aerogenes* infection, which responded to five days of terramycin therapy (2 gm. daily). The pelvic inflammatory disease subsided during the course of penicillin therapy.

A transient hypertension, 154/100, was noted on the fortieth day. After a transfusion of packed red cells on the fifty-first day, which increased her hemoglobin to 11 gm., dyspnea and basal rales recurred, and digitalis was resumed and maintained thereafter.

On the fifty-third day, serum electrolytes had returned to within normal limits. A twelve-hour urine-concentration test revealed a specific gravity of 1.009. A phenolsulfonphthalein-excretion test showed a total two-hour excretion of 10 per cent. An enlarged heart was shown on x-ray examination. The patient left the hospital against advice, to convalesce at home.

Discussion

The following factors may be of importance in the management of the phase of lower-nephron nephrosis when urine secretion is resumed and may progress to massive amounts:

Persistence of uremia, with nausea, vomiting and electrolyte imbalance, even though anuria is no longer present; *effects of massive diuresis*, with the development of multiple electrolyte and fluid depletion states; *effects of overtreatment* — an already overburdened circulatory system with deranged electrolyte concentrations may be further embarrassed rather than corrected by overzealous fluid and electrolyte therapy; *intercurrent disease*— the conditions existing prior to the onset of lower-nephron nephrosis and pulmonary or genitourinary-tract infections that may occur may be overshadowed by the more striking aspects of renal shutdown.

Persistence of uremia for two weeks after urine flow had begun was partly responsible for some of the complications encountered in this case.

The necessity of replacing fluid losses by the intravenous route resulted in overburdening of the circulation during the period of massive diuresis. The electrolyte imbalance and acidosis became even more marked when diuresis and "washing out" of electrolytes occurred. Overtreatment with both fluids and certain electrolytes such as potassium resulted from attempts to replace the losses of these substances. It soon became apparent to us that the period of diuresis was attended by as many dangers as the period of anuria had been.

In an attempt to prevent dehydration, it was decided to maintain fluid intake at a volume equivalent to output, which was calculated as total urinary volume plus 1000 cc. for insensible and other losses. Persistence of the uremic state for many days, with nausea and vomiting, made it impossible to administer fluids orally. When the diuresis reached massive proportions on the twenty-third day the volume of intake equal to the output proved excessive for the cardiovascular system, and pulmonary edema resulted. Strauss[1] has stated that when diuresis begins and the urine volume is in excess of 2 to 3 liters daily the danger of drowning the patient has become remote. Kroop,[2] however, has reported the occurrence of pulmonary edema during the diuretic period. When diuresis reaches the extent of 4 liters of urine in twenty-four hours it may prove dangerous to administer 5 liters of fluids, even if it is given slowly. The damage to the cardiovascular system during anuria, which may be due to anemia, hyperpotassemia or overhydration, may leave the circulatory system susceptible to failure if it is overburdened with intravenously administered fluids.

Derangements in calcium and phosphorus metabolism are common in uremic states.[3-12] The calcium-phosphorus ratio frequently becomes reversed, inorganic phosphates increasing while ionized calcium decreases, — probably because phosphate retention exceeds calcium retention and because phosphate loss into the gut is less than calcium loss in the stool and urine.[5] The occurrence of acidosis protects to some extent against the occurrence of tetany, since although the total serum calcium is reduced a greater proportion of it is ionized. Serial calcium and phosphorus studies were not made in this case prior to the onset of tetany, but calcium gluconate had been administered intravenously from the very beginning in doses of 2 gm. daily.[13-16]

The appearance of tetany after an intravenous infusion that contained enough potassium to raise the serum potassium level from 3.1 to 5.2 milliequiv. per liter suggests that an alteration in calcium-potassium ratio may have played an im-

portant part. Engel[17] has recently reported on the relation between the two ions, calcium and potassium, in the pathogenesis of this condition. Physiologically, their effects on the neuromuscular system are opposed. Either ionized calcium *depression* or potassium *elevation* may cause increased neuromuscular activity. Engel was able to produce tetany at will in a patient with hypocalcemia and hypopotassemia by administering potassium intravenously. The serum calcium, carbon-dioxide combining power and total protein values remained unchanged. When tetany occurred because of potassium administration, it could be abolished by the administration of calcium. Harbaugh and Dennis[18] report similar experiences in cattle. There is suggestive evidence, in fact, that a low serum potassium actually prevents the appearance of tetany due to hypocalcemia, and that in such cases increasing serum postassium disturbs the calcium-potassium ratio, increasing neuromuscular activity, and tetany follows. Engel therefore advises that administration of potassium to patients with hypopotassemia and hypocalcemia be accompanied by the administration of calcium to prevent the alteration in calcium–potassium ratio that leads to tetany.

Changes in serum pH also have a role in the production of tetany. It is possible that after pulmonary edema occurred hyperventilation resulted in an increase in serum pH, decreasing the concentration of ionized calcium to tetanic levels or to levels that, in combination with the recently elevated potassium, were responsible for the occurrence of tetany.

More remote factors that may have been involved in the pathogenesis of the tetany are: magnesium depletion[19] — a little understood mechanism, about which we have no information in this case; hyperguanidinemia, which has been suggested in acute and chronic uremia as responsible for tetany[20]; citrate toxicity[21] from the blood transfusion — which is not at all likely because of the small amount used and the long delay in the appearance of symptoms.

It appears, then, that the mechanism through which tetany probably occurred in this case was as follows: Hypocalcemia and hyperphosphatemia occurred in the course of renal shutdown due to a failure of the kidney to excrete phosphorus (and phosphorus rise from tissue breakdown), with greater loss of calcium into the gut and urine; chronic acidosis led to the ionization of a great part of the available serum calcium; pulmonary edema with hyperventilation resulted in a shift in serum pH toward the alkaline side, with decreased concentration of ionized calcium; potassium administration altered the calcium–potassium ratio, producing increased neuromuscular activity.

Repeated or continuous catheterization frequently is followed by urinary-tract infection, which may add further difficulties. The *A. aerogenes* infection in this case responded well to terramycin therapy. The pelvic inflammatory disease that was present at the onset of the renal shutdown cleared on penicillin therapy.

Summary and Conclusions

The complications of the diuretic phase of lower-nephron nephrosis may be as dangerous to the patient as the preceding period of anuria.

Uremia may persist far into the recovery phase.

Massive diuresis may result in water and electrolyte depletion states.

Attempts to prevent dehydration by intravenous replacement of the total volume of fluid lost may result in pulmonary edema even in the presence of massive diuresis.

In the presence of low serum calcium and potassium, administration of potassium may result in tetany unless calcium is administered simultaneously.

Intercurrent disease must be treated vigorously in addition to correction of fluid and electrolyte derangements.

We are grateful to Drs. Charles H. Burnett and Robert Tarail for their helpful advice and criticism.

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A TWENTY-YEAR HOSPITAL SURVEY OF DIABETIC DEATHS*

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THE shortcomings of medical therapy are highlighted by careful study of the records of deceased patients, and a most reliable guide for further improvement is thereby afforded. It is generally conceded that an autopsy is usually the ultimate in diagnosis. A careful study in a well appointed hospital approximates it, whereas a clinical opinion at a patient's home often only faintly resembles it. It is also commonly acknowledged that no amount of statistical skill can make a group of carelessly made observations accurate, no matter how large the series.

Death certificates of diabetic patients are subject to gross inaccuracies and omissions[1-4]; therefore a compilation of "facts" founded on them is often inferior to one based on a smaller number of hospital records that, in many instances, are fortified by autopsy protocols. "A fundamental condition of reliable statistics on diabetes in clinical practice is a set of good records."[4]

Some time ago an analytical study was made of all adult diabetic deaths at the Jewish Hospital during the interval 1930–1938.[5] Since that time the profession has entered an era of chemotherapy and antibiotic therapy that has profoundly influenced general medical progress. Another study covering the period 1939 through June, 1950, was therefore deemed advisable. All the records (1930–1950) were reviewed by the authors of this survey.

It should be noted that this institution is a general hospital of approximately 500 beds, expressly excluding the acute contagions, active open pulmonary tuberculosis and acute psychoses. Nearly all its patients are white and about 50 per cent are Jewish.

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EPIDEMIOLOGY

One hundred and fifty-five cases were surveyed in the original study; there are 247 in the more recent one. All cases were verified as diabetes mellitus by blood-sugar determinations or by history, or both. Although "the criterion most dependable for the identification of the disease diabetes is persistence of a tendency to elevation of the level of the blood sugar,"[6] such persistence could not always be determined — as, for example, in patients who died after a brief hospital stay.

In Table 1 is shown a compilation of all cases by age groups based on the onset of the diabetes. This is, of course, only an approximation, since recognition is often later than actual onset, the difference in time depending on the acuteness of the disease and the alertness of the patient. It will be noted that the age incidence has not varied materially in the past twenty years. It is difficult to draw any conclusions from this, since prophylactic measures widely recommended would tend to delay the onset of the disease, whereas diagnostic diabetes campaigns tend to induce earlier recognition. Women seem to acquire the disorder earlier in life. This im-

TABLE 1. *Age at Onset of Diabetes.*

Age	1930–1938					1939–1950				
	M	%	F	%	M + F	%	M	%	F	%	M + F	%
Up to 20	1	2.2	2	2.1	3	2.1	2	3.0	3	2.1	5	2.4
20–29	0	—	4	4.1	4	2.8	2	3.0	0	—	2	0.9
30–39	2	4.3	11	11.3	13	9.1	4	6.0	8	5.5	12	5.7
40–49	8	17.4	13	13.4	21	14.7	12	17.9	30	20.7	42	19.8
50–59	11	24.0	37	38.1	48	33.5	17	25.4	49	33.7	66	31.1
60–69	14	30.4	28	28.9	42	29.4	15	22.4	41	28.3	56	26.4
70–79	8	17.4	2	2.1	10	7.0	14	20.8	11	7.6	25	11.8
80 or over	2	4.3	0	—	2	1.4	1	1.5	3	2.1	4	1.9
	46	100.0	97	100.0	143	100.0	67	100.0	145	100.0	212	100.0
Unknown	6		6		12		13		22		35	
Totals	52		103		155		80		167		247	

TABLE 2. *Age at Death.*

Age	1930–1938				1939–1950			
	M	%	F	%	M	%	F	%
Up to 20	1	1.9	1	1.0	0	—	0	—
20–29	0	—	1	1.0	0	—	2	1.2
30–39	1	1.9	3	2.9	3	3.8	4	2.4
40–49	5	9.6	7	6.8	3	3.8	7	4.2
50–59	10	19.2	36	34.9	16	20.0	36	21.6
60–69	19	36.6	42	40.8	26	32.4	59	35.3
70–79	13	25.0	13	12.6	30	37.5	48	28.7
80 or over	3	5.8	0	—	2	2.5	11	6.6
Totals	52	100.0	103	100.0	80	100.0	167	100.0

pression is confirmed by actual compilation, the average age of onset for females being 52.5 years and that for males 59.0 years during the initial study and 55.4 years and 57.6 years respectively in the second one.

A breakdown of all deaths by sex and age is presented in Table 2. The sex ratio of females to males is about 2:1. This was also the experience of Joslin,[2] patients with diabetes mellitus in Boston in 1935.

The longer life of our patients is brought out in another manner in Table 3, in which an increase in the duration of the diabetes, from recognition to death, is seen. The average duration was 4.5 years for males and 6.7 years for females in our first study, whereas the corresponding figures for the next one were 7.3 years and 9.4 years. It is interesting to

TABLE 3. *Duration of Diabetes.*

	1930–1938				1939–1950			
	M	F	M + F	%	M	F	M + F	%
Not known on admission	12	22	34	21.9	15	13	28	11.3
Less than 1 yr.	9	10	19	12.3	2	6	8	3.3
1–5 yr.	13	21	34	21.9	16	33	49	19.8
6–10 yr.	7	24	31	20.0	14	46	60	24.3
11–15 yr.	5	7	12	7.8	9	17	26	10.5
Over 15 yr.	2	9	11	7.1	11	30	41	16.6
Inadequate history	4	10	14	9.0	13	22	35	14.2
Totals			155	100.0			247	100.0

Reed,[7] Drolet,[8] and Dublin and Lotka.[9] The National Health Survey of 1935–1936[10] and that of John[11] were likewise confirmatory, although living persons were surveyed. A smaller ratio or even a male preponderance has been reported,[12] but this is probably an artifact due to local selective conditions.[3]

The average age at death as found in our study of 1930–1938 was 63.5 years for males and 59.2 years for females, an overall average of 60.6 years. The comparable figures for the study of 1939–1950 were 64.9 years, 64.8 years and 64.8 years. Diabetic patients now apparently live longer. Such increases have been the experience of the George Baker Clinic,[3, 13] where the average age at death for all patients was found to be 62.7 years for 1930–1934, 63.9 years for 1935–1937 and 64.5 years for 1944–1946. Dublin and his co-workers[14] reported an average age at death of 67.0 years for white diabetic males and 66.8 years for similar females. Beardwood[15] surveyed all the diabetic deaths in Philadelphia during the years 1940–1942 and found the average age at death to be 64.3 years. This was the same figure obtained by Lynch[16] in a study of 301 patients with diabetes mellitus in Boston in 1935. The longer life of our patients is brought out in another manner in Table 3, in which an increase in the duration of the diabetes, from recognition to death, is seen. The average duration was 4.5 years for males and 6.7 years for females in our first study, whereas the corresponding figures for the next one were 7.3 years and 9.4 years. It is interesting to note that although the age at onset is younger in the average female, the duration of life with the disease is greater than for males.

Joslin[3] found that the average duration of diabetes was 14.1 years among 651 patients who died during the period 1944–1946. In Philadelphia, from 1940 to 1942, Beardwood[15] reported 7.5 years as the average duration.

CAUSE OF DEATH

The primary cause of death in each of our patients was next determined. Autopsies had been performed on 37.4 per cent of the patients in our primary series and on 34.8 per cent of those in the second one. Standard methods of nomenclature and classification were followed, except that the diagnosis of diabetes mellitus was given preference at all times. Minor changes were made in the interpretation of our previously published study to permit comparison with the more recent one. This comparative study is summarized in Table 4; striking changes are to be seen. In the past ten years the incidence of deaths due to pneumonia or other infections has decreased by 50 per cent. A similar decrease is seen in the

TABLE 4. *Cause of Death.*

AGE	1930–1938						1939–1950					
	M	%	F	%	M + F	%	M	%	F	%	M + F	%
Acute coronary thrombosis	3	5.8	5	4.8	8	5.1	15	18.8	35	20.9	50	20.3
Acute cerebral "accident"	3	5.8	13	12.6	16	10.3	9	11.3	24	14.3	33	13.4
Hypertension and "sclerotic" heart disease	9	17.3	17	16.5	26	16.8	19	23.7	22	13.2	41	16.6
All pneumonias	9	17.3	15	14.6	24	15.5	7	8.7	12	7.2	19	7.7
Other infections	10	19.2	15	14.6	25	16.1	4	5.0	16	9.6	20	8.1
Malignancy	3	5.8	4	3.9	7	4.5	4	5.0	14	8.4	18	7.3
Gangrene of legs	12	23.1	23	22.3	35	22.6	12	15.0	16	9.6	28	11.3
Diabetic coma	1	1.9	5	4.8	6	3.9	0	—	5	3.0	5	2.0
Blood dyscrasias	0	—	2	2.0	2	1.3	1	1.2	3	1.8	4	1.6
Others	2	3.8	4	3.9	6	3.9	9	11.3	20	12.0	29	11.7
Totals	52	100.0	103	100.0	155	100.0	80	100.0	167	100.0	247	100.0

frequency of deaths caused by gangrene of the legs and also of deaths due to diabetic coma. The incidence of acute coronary disease, however, shows a marked increase.

Pneumonia and Other Infections

The important role that infections have always played in the life of the diabetic is only too well known. Chemotherapy and the antibiotic drugs have markedly reduced mortality from infectious agents in general medical practice. It is only natural that the diabetic, with his lowered resistance to infection, should have benefited greatly from these modern therapeutic advances. Whereas 1 out of every 3 diabetic patients succumbed to a terminal infection during 1930–1938, only 1 out of every 6 patients was similarly stricken in our series of 1939–1950. In a group of 527 deaths reported by Warren[17] in 1938, 213 patients (over 40 per cent) died as a result of infection. For the interval of 1944–1946, Joslin[3] reports a 10.3 per cent mortality for similar patients. Progress in the introduction of specific and more widely available agents has been so rapid that therapeutic benefits available today are only partially reflected in statistics based on the past ten years; future studies should show even further statistical improvement.

Another and equally significant item has been the increasingly greater age of patients who finally succumb to some type of infection. This average age for our first study was 61.7 years for males and 58.2 years for females, an over-all average of 59.5 years. For the second study period the ages were 68.1 years, 62.5 years and 64.1 years, respectively. Despite this increase the average age at death is, as may be anticipated, still below that attained by the patients in the arteriosclerotic group to be described next.

Arteriosclerotic Diseases

Intimal sclerosis and plaque formation occur primarily in the vessels supplying the heart, brain, kidneys and lower extremities. The cardiac disorders produced are those referable to occlusion of major coronary vessels and an endarteritis of smaller ones leading to replacement of muscle by fibrous tissue, which eventuates in myocardial insufficiency. The obliteration of the glomerular arterioles results in nephrosclerosis, with its hypertension and cardiac hypertrophy. The overgrowth of connective tissue between the glomerular tufts, also resulting in glomerular obliteration, has been the subject of considerable study since it was so clearly described by Kimmelstiel and Wilson.[18] Although the syndromes produced are quite different, it is proper to consider them all under one pathological heading. "Regardless of where the peripheral artery is involved, the pathological picture is identical. It is thus impossible to differentiate pathologically an arteriosclerotic coronary artery from an arteriosclerotic popliteal artery."[19] In the diabetic the arteriosclerotic process is almost uniformly found in the coronary vessels and in those of the lower extremities, the intima of other vessels being affected only with the same frequency and intensity as would be expected in a nondiabetic.[20]

In our original series of 155 patients, vascular sclerotic disorders accounted for 85 deaths (54.8 per cent). The more recent series of 247 cases revealed that 152 patients (61.6 per cent) died of arteriosclerotic disease, this despite the tremendous diminution in the number of fatal cases of gangrene of the legs. The average age at death was 63.3 years in the first group and 65.4 years in the second one.

Beardwood[15] found arteriosclerosis to be responsible for 44.8 per cent of the diabetic deaths in Philadelphia, whereas Lynch's[16] comparable figure was 59.5 per cent for Boston.

Gangrene of the Legs

Although the vascular endarteritis seen in the legs of a nondiabetic is primarily the same as that of the diabetic,[6] the latter shows a greatly accelerated process, and gangrene of the lower extremities therefore has always been a dreaded complication of diabetes. It is particularly gratifying to note that this vascular disease has been markedly reduced as a cause of death in our series of the past ten years. Modern improvements in surgical and medical management of peripheral vascular disorders probably were largely responsible. The serious influence of infection in further reducing the diminished blood supply of the diabetic to the level of onset of gangrene has been commented on by Joslin,[3] Wilder,[6] Warren[17] and Wirtschafter and Korenberg.[21] During the period from 1923 to 1942, McKittrick[22] performed 609 major leg amputations in patients afflicted with diabetes, with a mortality of 14.1 per cent. With the identical technics supplemented by ample supplies of antibiotics, the mortality in the next 212 cases was reduced to 4.7 per cent. Antibiotics therefore should also be given much credit for the reduction in deaths from gangrene. From a figure of 1 out of every 5, deaths caused by gangrene of the leg have been reduced to 1 out of every 10.

Twenty-four male deaths due to this cause (18.2 per cent) and 39 female deaths (14.4 per cent) were noted. The average duration of the diabetes was increased from 7.4 years in our original group to 10.8 years in the next one. It is the experience in many peripheral-vascular clinics that men are far more subject than women to vascular disorders of the legs but the male preponderance is smaller among diabetic patients.[6, 23, 24]

Of 429 post-mortem examinations performed on diabetic patients at the Baker Clinic from 1923 to 1945,[3] 53 patients (12.4 per cent) were primarily the victims of gangrene of the leg. Warren[17] re-

ported 88 cases of such gangrene among 527 autopsies.

Acute Coronary Thrombosis

The incidence of severe coronary disease has been consistently greater. This is due partly, or perhaps entirely, to greater diagnostic accuracy and to the fact that increasing frequency of sclerotic vascular disease is to be anticipated in a population whose older segment is constantly growing in size. In our study of the past ten years, acute coronary thrombosis has supplanted infection as the most frequent cause of death in patients with diabetes, and it was present as the fatal condition in 1 out of every 5 such patients. Palmer[25] also lists this condition as the most common cause of death in patients known to have diabetes. Dry and Tessmer,[26] reviewing 139 autopsies in patients with diabetes who died during 1925–1936, found that 15 of them (11 per cent) died of acute coronary thrombosis. Joslin[3] noted 93 cases (21.7 per cent) of acute coronary thrombosis among 429 autopsies. Warren[17] found acute coronary thrombosis in 16.4 per cent of his series of autopsies, and Beardwood's[15] survey showed a similar condition in over 15 per cent of patients.

There were 18 males and 40 females in our series of coronary deaths — practically an equality of percentage incidence of the sexes. In reviewing a group of 1500 consecutive general medical deaths at this hospital for the years 1930–1939,[27] twice as many coronary deaths were noted in males as in females. This was also the finding of Hedley[28] in Philadelphia. The increased frequency of severe coronary disease in diabetic women has also been noted by Wilder[6] and by Root and others.[29]

Diabetic Coma

Of all the many complications of diabetes, acidosis with coma is probably the least justifiable, in view of the availability of insulin, which is both a specific prophylactic agent and a cure. The persistent small percentage of these fatalities constitutes a challenge, as it represents either lack of co-operation from the patient, failure to recognize the presence of diabetes, or failure to diagnose and treat intercurrent infection, often genitourinary.

Deaths from diabetic coma are particularly distressing to note, as they usually represent a marked shortening of the expected life span. Of the 11 patients in our entire series who died in coma due to diabetic acidosis, 7 patients were 40 years old or less at death. Four of our coma patients were not previously known to be diabetic.

Insulin Dosage

In the course of our study, it was thought that a correlation of insulin dosage with the final cause of death might reveal significant information. The dosage in question was, of course, the one in use just prior to the onset of the terminal condition (Table 5).

Table 5. *Insulin Dosage Prior to Onset of Terminal Illness.*

Diagnosis	No Insulin	25 Units or Less	Over 25 and Under 50 Units	50 Units or Over	Subtotals	No History	Totals
Gangrene of legs	(37.3%) 22	(35.5%) 21	(13.6%) 8	(13.6%) 8	(100.0%) 59	4	63
Hypertension and arteriosclerotic heart disease	(47.4%) 27	(38.6%) 22	(12.3%) 7	(1.7%) 1	(100.0%) 57	10	67
Acute cerebral "accident"	(37.2%) 16	(39.6%) 17	(20.9%) 9	(2.3%) 1	(100.0%) 43	6	49
All infections	(65.0%) 52	(23.7%) 19	(10%) 8	(1.3%) 1	(100.0%) 80	8	88
Acute coronary thrombosis	(53.1%) 26	(30.6%) 15	(12.2%) 6	(4.1%) 2	(100.0%) 49	9	58
Diabetic coma	(70.0%) 7	0	(20.0%) 2	(10.0%) 1	(100.0%) 10	1	11
Others	24	20	12	3	59	7	66
Totals	(48.7%) 174	(31.9%) 114	(14.6%) 52	(4.8%) 17	(100.0%) 357	45	402

Only half the diabetic patients were on any insulin regimen — and most of these were taking less than 50 units daily. It is usually stated that high insulin dosage should be avoided and that many patients require no insulin at all. However, the indiscriminate failure of the diabetic to take any insulin at all until he is critically ill is perhaps even more serious, since it seems highly significant that no insulin was being taken at the time of death in an unusually high percentage of cases with deaths from infections or diabetic coma. The great progress that has been made in insulin therapy should not be negated by a stubborn reluctance to "take a needle."

In his text, Wilder[6] states that 30 per cent of all diabetic patients need 30 units or less of insulin daily and 14 per cent require more than 30 units daily. Apparently the remaining 56 per cent are taking no insulin at all. This corresponds fairly well with our own findings.

Cholelithiasis

No general discussion of diabetic disease is complete without some mention of gall-bladder disease — and, more particularly, of gallstones. In a group of 746 autopsies performed on adults at this hospital, gallstones were found to be present in 11.9 per cent.[30] Among 144 diabetic patients who also were autopsied here, 40 patients (27.8 per cent) had gallstones. In similar patients the percentage was found to be 31 per cent by Warren,[17] 28.0 per cent by Wilder[6] and 35.2 per cent by Schleusner.[31]

When our figures are broken down, however, it is found that whereas the incidence of gallstones among women with diabetes was 37.2 per cent it was only 12.5 per cent among men. The comparative incidence in nondiabetic patients was found to be 15.0 per cent and 9.3 per cent respectively in the same institution.

Summary

A careful study was made of the hospital records of over 400 patients who had diabetes mellitus and who died during the period 1930 through June, 1950. Several epidemiologic features of the disease were studied and conclusions were drawn, the most significant being an increase in length of life for our patients since 1938.

The primary causes of death were compiled for all patients. These were then arbitrarily divided into two groups according to the date of death, 1930–1938 and 1939–1950. It was found that there was a marked diminution in infectious deaths in the second group, which was attributed to the generous use of antibiotic drugs that were available during that period. The number of deaths due to gangrene of the leg was likewise diminished, but deaths due to other forms of vascular sclerosis, particularly acute coronary thrombosis, were increased.

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FIFTY YEARS OF MEDICAL PROGRESS

MEDICINE AS A SOCIAL INSTRUMENT: JOURNALISM

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EVEN in 1939, still in that half-forgotten era prior to World War II, Sir Robert Hutchison estimated the current global crop of medical periodicals at between 5000 and 7000, of which about 130 were published in Great Britain alone.

Sir Robert, however, did not condemn medical literature because of this fecundity or advocate any form of planned parenthood. He merely stated the aphorism "that the amount of the writings of a profession is a measure of its vitality and activity, whilst their quality is a rough indication of its intellectual state." With comparable judgment he weighed in the balance the usual motives for writing:

> Good reasons are the necessity for putting on record new observations or results of experiments and the impulse to teach — to impart a conviction or to present a subject in a new light. Bad reasons are the desire for prestige and priority (of which the "preliminary note" is a familiar example) or the itch for advertisement.

The reasons for publishing journals and for contributing to them have probably changed little over the years; it is the mode of expression, the style, the format, the scientific problems and the burning issues that have changed from one period of time to another. The same human impulses and desires and ambitions continue to operate; it is the technics of trying to gratify them that are in a constant state of flux, call it progress or what you will.

Certainly the volume of medical periodicals has increased, even since Hutchison made his comments on medical literature, but the population of the world has increased also, and the number of physicians to care for its ills and comfort it, and the facilities that they have at their command; there is much in medicine to write about — and much has been written about it.

The consideration of even so short a period as fifty years may take on added meaning if viewed in the light of what preceded it; the present plays its part before the backdrop of the past, and a résumé of medical journalism even prior to the twentieth century may be of interest.

The first medical journal to be published in the world began its brief life in Paris in 1679. This was *Nouvelles Découvertes sur Toutes les Parties de la Médecine* (becoming *Zodiacus Medicus* in the following year), which appeared under the proprietorship of Nicolas de Blegny and continued publication until 1683, exhibiting considerable stamina for the genetic mutation that had originated this new species of literature. The century was ripe, however, for such an experiment. Harvey's *Exercitatio anatomica* had been published in 1628, the Royal Society had been chartered in 1662, and in 1664 the publication of the society's *Philosophical Transactions* had begun, to continue to the present day. The human race had entered the Age of Reason, and the world was full of curiosity and eagerness.

The *Zodiacus*, infectious in nature, was the first case in a small epidemic of medical publications that seemed to have an incubation period of between one and two years. The second case appeared in Holland in 1680 and the third was of German origin, erupting in 1682. The fourth journal to appear, — and the first in the England language, despite its Latin title, — was *Medicina curiosa*, a quarto of 56 pages, the first issue of which was published on June 17, 1684. The second appeared on October 23 of the same year, but the effort was too great and it forthwith expired.

Medical journalism, however, had been launched and could not be held back. These first attempts were followed by others, like popcorn bursting into bloom over a fire, until finally a more stable form of journalism came into existence to satisfy the demands, we may suppose, of its potential readers. The infant mortality continued high, nevertheless, as with all new enterprises.

Ninety-three years passed since de Blegny's noteworthy experiment before anything that could rightly be called a medical periodical appeared in the New World. Then, not in Boston or Philadelphia or New York, but in Mexico City, on October 17, 1772, *Mercurio volante* started rolling off the presses and continued to roll at frequent intervals until with the sixteenth issue in February, 1773, its revolutions ceased.

Nothing that could in any sense be called a medical journal antedated the flying mercury of this country's southern neighbor, although in 1677 there had been published in Boston the earliest known medical essay of any sort in the western hemisphere. This was *A Brief Rule to guide the Common People of New England How to order Themselves and theirs in the Small Pocks, or Measels* and was signed, after a brief supplication to the Lord to turn our hearts and stay his hand, by "A Friend, Reader to thy Welfare, Thomas Thacher."

A hundred and thirteen years were to pass after the appearance of Thomas Thacher's pious reflections on smallpox (or measles) before a series of

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weighty, dignified and altogether important publications began to be printed in New England. These were the *Medical Papers Communicated to the Massachusetts Medical Society, to which are subjoined extracts from various authors, containing some of the improvements which have lately been made in physic and surgery*. These transactions, appearing first in 1790, were published from time to time until 1914, when their function was taken over by the *Boston Medical and Surgical Journal*. However, they did not in themselves represent an attempt at medical journalism north of the Rio Grande. This was to come in 1797, when the *Medical Repository* appeared in New York, continuing its sober career until 1824, overlapping the establishment of at least four journals that are still current.

Morris Fishbein, at the time editor of the *Journal of the American Medical Association*, in an address delivered at the hundredth anniversary of the birth of the *Boston Medical and Surgical Journal*, attributes some eighty medical periodicals to the industry of eighteenth-century medical editors. Of these, 55 were German, 4 were English, 3 were French and 1 was American.

The journals of the seventeenth and eighteenth centuries are literary curiosities as viewed from the lofty position occupied by the intellectually and socially privileged physician of the mid-twentieth century. All are gone, and most of them are forgotten. The nineteenth century, however, presents another story, for in its early years a succession of journals were established of which a few survived for many years, — some even to the present day.

The *Edinburgh Medical and Surgical Journal*, the dean of all the journals still current, came into being in 1805. Eighteen years later, what has been fittingly termed the new era in journalism was inaugurated in London by the *Lancet* — a crusader's lance rather than a surgeon's scalpel, — designed not only for the diffusion of knowledge but to raise educational standards and to correct abuses, and to remain, for a few decades at least, in an intermittent state of controversy.

The *New England Journal of Medicine and Surgery and the Collateral Branches of Science, Conducted by a Number of Physicians*, had already made its debut in Boston as a quarterly periodical in January, 1812. The title of the first paper in the infant journal, "Remarks on Angina Pectoris," by John Warren, established for all time the high standards of this remarkable publication.

The journal was started under excellent auspices, having been proposed by John Collins Warren, who united with himself in the enterprise James Jackson, John Gorham, Jacob Bigelow and Walter Channing. The editorship passed entirely into the hands of Dr. Channing and Dr. John Ware in 1824, and in 1827 the name was changed to the *New England Medical Review and Journal*.

Meanwhile, almost synchronously with the advent of the *Lancet*, the Boston *Medical Intelligencer* appeared as a weekly publication. Despite the devastating rapidity with which seven days can elapse, the *Intelligencer* remained faithful to its deadlines until February, 1828, when it was purchased by Drs. Warren, Ware and Channing for the sum of $600 and was united with the *New England Medical Review and Journal*.

As a result of this union an interesting event took place, which was announced on February 12, 1828, in the *Intelligencer* in the following words:

> On Tuesday, next week, will appear the first number of the *Boston Medical and Surgical Journal*, as a continuation of this paper. When we consider the number, the talents, and experience of the Editors of the forthcoming journal, and their abundant resources for matter, we cannot doubt that this paper will prove generally acceptable, because we feel an assurance that it must be interesting and useful.

Thus what may be considered our own journal came into existence and has continued in circulation ever since, not only without the drop of a systole but even with a partial reversion to its ancient title on its hundredth birthday.

The other notable periodical to be born in this decade, which saw also the births of Pasteur, Lister, Elizabeth Blackwell, Florence Nightingale and Clara Barton (among others), was the *Philadelphia Journal of the Medical and Physical Sciences*. This distinguished publication appeared first in November, 1820, changing its name seven years later — "in order to emphasize the more national character of the journal" — to the *American Journal of the Medical Sciences*.

During the nineteenth century, journalism of necessity kept pace with the advances of medicine, and the renaissance of medicine as a science was truly under way. As in the eighteenth century, when they had 55 journals to their credit, the Germans took the lead in productivity. Virchow's *Archiv für pathologische Anatomie* was founded in 1847 and was followed by the establishment of a considerable number of prominent periodicals.

In England the *British Medical Journal*, one of the four current weeklies of note in the English language, began its career in 1857 "with a comprehensive editorial policy extending even to such subjects as that of sea-bathing in the Serpentine, which was to be filled with salt water." The early editorials or leading articles, like those of the *Lancet*, covered a variety of subjects.

In 1858, as a pleasant excursion into the byways related to health, an editorial (or leading article) in praise of roast beef appeared, with notes on the methods of fattening it, as well as one on Frugal Marriages, whose only reference suggestive of medicine was "that neither frugal marriage nor luxurious celibacy have anything to do with the successful practice of physic."

Meanwhile certain weighty events were transpiring in this country. The American Medical Association was founded in 1847, a committee on medical literature being appointed at its first meeting, consisting of Oliver Wendell Holmes, Enoch Hale, G. C. Shattuck, Jr., Daniel Drake, John Bell, Austin Flint and W. Selden, to prepare "an annual report on the general character of the periodical medical publications, on medical compilations and compends by American writers, on American reprints of foreign medical works, and on all such measures as may be deemed advisable for encouraging and maintaining a national literature of our own."

FIGURE 1. *John Shaw Billings. (Reproduced from Hume, E. E. John Shaw Billings as an Army Medical Officer.* Bull. Johns Hopkins Hosp. *62:237-282, 1938, by Permission of the Publisher.)*

Not necessarily as a result of the committee's profound deliberations, the *Transactions of the American Medical Association* were conceived, giving way thirty-six years later to the *Journal of the American Medical Association*, whose first issue appeared on July 14, 1883. With this event, according to Postell, modern medical journalism came into existence, — a challenging statement when one considers that the fledgling had to meet the competition of over 860 journals that were by then in circulation.

During this period not only did the *Boston Medical and Surgical Journal* continue to pursue the noiseless tenor of its way, having changed its form to two columns in 1868 (the editors hoping that by this device it "will conform somewhat in shape and appearance to the best modern specimens of hebdomadal literature"), but other familiar names appeared.

In 1866 the *New England Medical Gazette* entered the course as the official organ of the Massachusetts Homeopathic Society, to continue in publication until 1918, and the *Practitioner* began in London a career that has continued to the present. Meanwhile the trend toward specialty journals that had begun with Virchow's *Archiv* continued to grow in importance. Of note among these are the *Journal of Anatomy and Physiology*, established in 1866; the British *Brain* and the *Journal of Physiology*, which made their appearance in 1878, the *Journal of Laryngology and Rhinology*, of the vintage of 1887, and the *Journal of Pathology and Bacteriology*, which had its advent in England in 1892.

A patriarchal practitioner in contrast to these specialists was the *New Orleans Medical Journal*, established in 1844, which, after operating under a number of aliases, reverted to the title of *New Orleans Medical and Surgical Journal*, in 1870, started a new series in 1873 and has continued in publication ever since, being at present the official organ of the Louisiana State Medical Society.

Thus a number of mid- and late-nineteenth-century journals, in addition to the ancient quartet of the *Edinburgh Medical Journal*, the *New England Journal of Medicine and Surgery*, the *Lancet* and the *Philadelphia Journal of the Medical and Physical Sciences*, have bridged the period between the old and the new and linked the medical progress of the nineteenth century to that of the first half of the twentieth.

It would be folly, in a brief narrative of this nature, to attempt any analysis of world medical literature or, indeed, to mention specifically more than a few of the journals that have chronicled the progress of the Golden Age of medicine. The oversights and omissions, if thoroughness were attempted, would stand out too glaringly. The stream of medical progress that received so much increment during the nineteenth century has widened to the point where names no longer count, so numerous are the voyagers who now navigate its currents. This flood of scientific achievement has added to the intricacy as well as the volume of the literature that chronicles it.

Hutchison's estimate of the number of journals current in 1939 has been mentioned; his 5000 to 7000 periodicals may be contrasted with the figure given in 1880 by John S. Billings, director of the Army Medical Library (Fig. 1), of 864, of which

506 were considered to be general and miscellaneous in nature. Sanford V. Larkey, librarian of the Welch Medical Library of Johns Hopkins Medical School, commenting further on this growth, stated last year that the *Current List of Medical Literature*, published by the Army Medical Library, consisted of 1286 journals, of which only 315 were general in nature, and ventured a guess that there are in the world today between 8000 and 10,000 journals devoted to medicine and the related sciences.

Hutchison, disturbed although not prostrated by contemplation of this continually rising stream, exclaimed, "Must we sit still and see science suffocated in its own secretions, or can we do anything to mitigate the evil?"

As evidence that the benefits of such a river of learning are not universally appreciated, he tells of entering the study of a practitioner, a man well read in general literature, and seeing on the floor a large heap of weekly medical journals still enclosed in their wrappers. "On my asking him why he kept them there if he did not mean to read them, he replied that he found them useful to throw at the cat!"

Another Hutchisonian anecdote à propos of this state of affairs is that of a young physician

> who went down to act as holiday locum for a practitioner in the country. The practitioner before leaving told the young man that he would have the run of the house except for one room which he must not enter. Needless to say, no sooner had the holiday-maker gone off than the young man made his way into this Bluebeard's chamber only to find it stuffed from floor to ceiling with unopened medical journals. Such was the elderly practitioner's grisly secret.

Periodical medical literature, however, has obviously changed in this half-century, in ways other than in volume, and has made growth that is not entirely a matter of numbers. Much of this change has been salutary; it is in keeping with the times; it is maturing even as medical science, whose mouthpiece it is, has developed. It has its shortcomings and its problems as well.

The outstanding feature of this expansion has been the tremendous increase in the number of specialty journals. Beginning, so far as modern medicine is concerned, with the birth of cellular pathology and Virchow's *Archiv für pathologische Anatomie*, it broadened into the dignified list of journals more or less representative of the basic medical sciences and the recognized subdivisions of practice that have already been mentioned, and many others, equally meritorious, have followed.

With the beginning of the twentieth century and the increasing sophistication of medical practice and medical research there came the craving of each minute and detailed branch of medical learning to have its own systems of communication, and the modern race began.

Many of these specialty journals, covering the activities of medical practice and medical science from abdominoscopy to zymology and perhaps beyond, are extremely important in the specialties that they represent, and all of them are unquestionably serious in purpose and more or less vital to the groups, however small, that they serve. It must be admitted, nevertheless, that they tax the facilities of libraries, make nightmares of the once scholarly pursuits of indexing and abstracting, and must cause financial headaches beyond the power of any salicylate to assuage.

As has been mentioned, of last year's *Current List* of nearly 1300 journals — perhaps not over an eighth of the total published — 971 were the property of the burgeoning specialties and only 315 were assigned to the category of general medicine. Seventy years before, of the 864 journals listed by Billings 358 were in the domain of specialism and 506 pertained to general, miscellaneous and "practical" medicine.

So detailed, in fact, has this riotous efflorescence become, with journals devoted to circulation and to the blood of the circulation, and to the heart that starts the blood on its circulatory course; with journals on the anatomic predilections of disease, on detailed forms of treatment and on specific technics of diagnosis, that the general practitioner, that *avis* who is not so *rara* after all, has been driven to the wall. In self-defense he has been forced to make what remains to him of the art of medicine a sort of general specialty by decree, and, shunning the publications that have served his ends for these many years, he has established still another journal, — specialized, if not of a specialty.

Another trend that has certainly shown its greatest expansion in the past half-century has been the development of a class of journals as the official organs of societies and other groups whose members are bound together by common interests. In this country the journals of state medical societies had their origin in the latter part of the last century and have increased to the point where 46 of the states are now represented by 38 journals. It is a matter of local interest that the Massachusetts Medical Society in 1914 arranged with the owners of the *Boston Medical and Surgical Journal* to make that periodical its official organ and in 1921 purchased it outright and has continued its publication ever since. The *Journal* is also the official publication of the New Hampshire Medical Society.

But, like the fleas on the dog, this sponsorship does not end with the state societies and those learned organizations less political in nature. Many of the district societies have their bulletins devoted to the common good, and many of the medical schools and their alumni associations and student organizations as well, to say nothing of hospitals and clinics, have their own publications, more or less scientific and many of unusually high caliber.

Larkey, in his analysis of 800 journals in the Welch Medical Library, notes this high degree of society sponsorship, amounting to 590 journals or 74 per

cent of the whole. This is particularly evident in the English-language periodicals, 317 or nearly 80 per cent of 397 journals published in the United States being thus sponsored. This fact, desirably or otherwise, accounts for the survival of so many journals in the midst of so much economic stress.

Accompanying this variegated profusion of professional periodicals are still other echelons to make up a formidable task force — the journals of medical history and those dedicated to the further in-

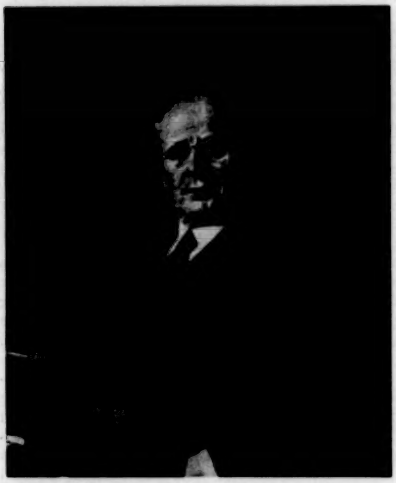

FIGURE 2. *George Henry Simmons.* (*Reproduced from* Testimonial Banquet with Presentation of Portrait to Dr. George Henry Simmons on his Twenty-Fifth Anniversary as Editor of the Journal of the American Medical Association. *Frontispiece. Chicago: American Medical Association, 1924, by Permission of the Publisher.*)

formation of medical librarians; journals of military medicine; and last and most insistent in their ability to reach the practitioner's desk, because they are free, the journals that owe their existence to the commercial interests that sponsor them. Nor are these journals that originate in the busy marts of commerce of no value. Given over to economic advice, analyses of socio-medical problems and abstracts of current literature and profusely interlarded with advertisements, the "throw-away" journal is often perused before being discarded, even while the scientific periodicals accumulate, unopened and unread.

Meanwhile the "all-purpose" journals, whether independent and presumably self-supporting like the *Lancet* and the *Practitioner*, or the bondservants of prosperous societies, like the *British Medical Journal*, The *Journal of the American Medical Association* and the *New England Journal of Medicine*, have kept abreast of the times and have continued to broaden their interests and increase their usefulness.

So important have the social and medico-political obligations of the latter group become, however, that cleavages between the scientific and the more heterogeneous material are becoming increasingly desirable. The *British Medical Journal* publishes its political material in a supplement, and the *New England Journal of Medicine* has recently adopted an even more radical measure, that of printing and distributing the proceedings of the Society in a completely separate section.

The *Journal of the American Medical Association*, covering a wide diversity of interests, may soon have to undergo some similar type of mitosis.

What has happened to the *quality* of medical writing in the last fifty years? Fishbein believes that the development of "style" in this country was a contribution of Dr. George Henry Simmons (Fig. 2) after he assumed the editorship of the *Journal of The American Medical Association* in 1899. Certainly standards have been set and precedents established that when observed have raised the level and improved the uniformity of medical literature.

Fishbein has himself made a considerable contribution in this direction with the preparation of his small but highly nutritious volume on *Medical Writing*, first published in 1938 and now in its second edition. The American Medical Writers' Association has also for its purpose the improvement of the quality of current medical literature.

The British, perhaps because of better academic education, perhaps because of a literary and cultural background that goes farther and deeper than our own, usually make a better fist at their medical writing. It may be that in England eight out of every ten physicians do not feel called on to measure their professional success with the foot rule of literary output; it may be that in America the compulsion to write to maintain academic standing or to advertise one's accomplishments in a genteel and ethical manner is stronger than it is elsewhere.

And here, also, Hutchison has his pertinent observations to make, listing medical literature in general as "too long, too dull, prolix and obscure," American literature offending particularly in prolixity and obscurity.

"Was there ever yet anything written by man," he quotes Dr. Johnson as saying, "that was wished longer by its readers excepting *Don Quixote*, *Robinson Crusoe* and the *Pilgrim's Progress*?"

There is, at least in the medical literature of this country, an overelaboration of data with an increasing, as well as a much sounder use, it must be admitted, of biostatistics. Too frequently the im-

pression is gained that the urge to demonstrate the writer's knowledge exceeds the desire to improve that of the reader.

Dr. Robert W. Buck, in analyzing the trends of the period in the type of material presented, found that in the first volume of the *Johns Hopkins Hospital Bulletin*, published in 1890, original work made up 30 per cent; in 1949 it constituted nearly 60 per cent. The *Journal of the American Medical Association* in 1900 devoted 30 per cent of its space to original work and 65 per cent in 1949. "In the other journals there were many contributions that could be classified under the heading 'Experience and Advice,' from older men of established reputation; in the contemporary journals the spirit of busily competitive activity is apparent; the dominant note is that of ambitious youth."

On the whole the journals, particularly in the upper brackets, show better editing; the illustrations of course show constant improvement; the editorials and editorial policies, while quite naturally supporting the professional point of view, when dealing with controversial matters, are keeping up with the changing times.

Mention should be made, in listing the advances of medical journalism, of the publication of the clinicopathological conference — the "organ recital" of undergraduate parlance. In whatever remote period of history this frank posting of the books of medicine had its origin, much of the credit for its popularity belongs to Dr. Richard C. Cabot.

The story of the Cabot Case Records of the Massachusetts General Hospital goes back to 1895, when Dr. Cabot began using printed case histories of the hospital in his teaching exercises. In 1911 the cases and their discussion — in view of the postmortem or operative findings — were first published independently; in 1923 the publication was taken over by the *Boston Medical and Surgical Journal* and has continued under the same auspices ever since.

This method of instruction has had wide popularity, and many similar series of cases are now published. As Dr. Alan Gregg, director of medical sciences of the Rockefeller Foundation, wrote in 1938 ". . .The clinicopathological conference is the wonder of many of our foreign visitors, who see in it a candor and fearlessness altogether to the credit of American medicine."

Medical journalism, like all unfinished business, has its continuing and its new problems. *Indexing* was called by Oliver Wendell Holmes, the elder, a founder of the Boston Medical Library, the supreme need of medical literature. The need has grown as the volume of writing has increased, to the point where the *Current List of Medical Literature* expects soon to record 90,000 articles a year, called from the approximately 200,000 published.

The *Index Medicus*, as an activity of the Army Medical Library, representing a justifiable function of the government, was established by Billings in 1879. In 1880 he began also the publication of the Library's *Index Catalogue*. In 1927, financially neglected by Congress, the *Index Medicus* was forced to consolidate with the *Quarterly Cumulative Index* of the American Medical Association. In latter years the *Quarterly Cumulative Index Medicus*, overwhelmed by the flood of literature, has fallen far behind in its task, being at present, as Fishbein expresses it, neither quarterly nor cumulative.

A number of countries have their own relatively complete medical indexes; the international problem is under investigation by two agencies. One of these, the Committee on Indexing and Abstracting of Medical Literature, of the Division of Medical Sciences of the National Research Council, is carrying on its preliminary investigations in the Welch Medical Library in Baltimore. The other is the Committee for the Coordination of Abstracting and Indexing in the Medical and Biological Sciences, of the United Nations Educational, Scientific and Cultural Organization (UNESCO). This committee, under the chairmanship of Dr. Hugh Clegg, editor of the *British Medical Journal*, is trying at least to uncover the whole problem. Its first plan of action is the publication of an international list of medical journals with uniform abbreviations, which it is hoped will be internationally acceptable.

Parallel to the problem of indexing each year's literary precipitation is that of trying to abstract those articles that merit preservation in tabloid form. This service was well performed in Germany prior to the first world war; since that event various publications have attempted it, none of which have been entirely satisfactory. In addition to over 70 journals of abstracts alone received at the Welch Library, more than 500 journals not classed as abstract journals nevertheless publish abstracts in addition to their other material. The unnecessary duplication can be imagined.

Since the second world war, two important abstract services have been developed — the British *Abstracts of Medicine and Surgery* and the Dutch *Excerpta medica*, published in English and considered to be the one that comes nearest to meeting the requirements of a satisfactory abstract service in this language. Its task, however, is that of trying to plow a road while the blizzard is still raging. The matter of storage of this literary output, aside from its indexing and abstracting, is still another problem. One promising line of attack is the microfilming of current journals instead of binding them.

In advertising, and particularly in the ethics of advertising, progress has also been made in this half century. Prior to 1905, advertising in medical journals was largely a matter of first come, first served, but in that year the American Medical Association established its Council on Pharmacy and Chemistry as a standing committee "to combat irrational medication and the distribution of worthless preparations," and something in the nature of a new conscience became operative. No drug is now

accepted for advertisement in publications of the American Medical Association and in other publications operated under the same policies unless it has been approved by the Council.

The Co-operative Medical Advertising Bureau was organized within the American Medical Association in 1930 to procure advertising contracts for the journals of the state societies. Thirty-four of the 38 state journals subscribe to the bureau, now called the State Journal Advertising Bureau, and participate in its benefits.

Other journals monitor their own advertisements, more or less strictly; the *Annals of Internal Medicine*, for instance, published by the American College of Physicians, has set up its own committee on advertising to widen a little the limits established by the Council on Pharmacy and Chemistry, which some publishers consider unnecessarily rigid. In Britain the Medical Journals Watch Committee, operating under 12 items of policy, governs the advertising in the *British Medical Journal*, the *Lancet* and the *Practitioner*.

At the moment of writing, periodical medical literature is sharing the same hazards that attend all forms of human enterprise. The times are uncertain, prices are high and paper is again becoming a relatively restricted commodity. The degree of security afforded by sponsorship and the specialized activities of co-operative advertising organizations is a blessing that does not need to be disguised.

There are too many medical journals, of course, and too much medical literature in the free world, but so long as original work is being done and the desire to tell about it and the privilege of doing so remain uncurbed, the Golden Age of medicine has not yet reached its end.

The author gratefully acknowledges the assistance of the staff of the Boston Medical Library, the editorial board of the *Journal* and others.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 37221

PRESENTATION OF CASE

A forty-nine-year-old man entered the hospital complaining of severe abdominal pain.

Four years prior to admission the patient began to have frequent attacks of "grabbing" substernal pain occurring with exertion or emotional stress. These were relieved by nitroglycerin tablets, of which the patient usually took 12 or 14 each day. He also noted the onset of exertional dyspnea of such a degree that climbing one flight of stairs became a major effort. Three years before admission the patient entered a community hospital complaining of dyspnea, orthopnea and ankle edema. Nine months before admission he was readmitted to the same hospital because of severe, persistent chest pain. He was digitalized at this time and was maintained on small daily doses of digitalis thereafter.

On the evening of admission the patient ate a meal that included fat pork. Shortly thereafter, while riding to work on a train, he suddenly developed a severe, dull, pressing pain extending across the abdomen at the level of the umbilicus that was not relieved by nitroglycerin or by Pepto Bismol. The pain was accompanied by cold sweat and extreme apprehension, but there was no nausea or vomiting. During the next three or four hours the pain radiated to the subxiphoid region and continued to be so severe that the patient came to the Emergency Ward, where 100 mg. of Demerol and 30 mg. of morphine afforded only partial relief.

For many years the patient had had occasional mild postprandial distress after eating bacon or cabbage. However, his appetite was good and he had had no weight loss. For several years there had been urinary frequency and three- or four-times nocturia. He had had an appendectomy at the age of twenty-five years and five attacks of pneumonia at ages twenty, twenty-three, forty-four, forty-six and forty-seven years. His mother died of diabetes at the age of fifty-nine years.

Physical examination revealed a heavy-set, florid-faced middle-aged man who was perspiring profusely and was unable to sit still in bed because of subxiphoid pain. The neck veins were flat. The lungs were clear to percussion but diffuse rhonchi and moist inspiratory rales were heard. The heart was enlarged to percussion and had a regular rhythm with occasional extrasystoles and runs of pulsus alternans. The rate was 100. The sounds were distant and of poor quality. The pulmonic second sound was much louder than the aortic, and a high-pitched, blowing apical systolic murmur was heard. The abdomen was soft and contained no masses. There was minimal tenderness along the right costal margin and below the xiphoid on direct palpation, but there was no rebound tenderness. Peristaltic sounds were active and of normal pitch. There was no peripheral edema. Neurologic examination was unremarkable.

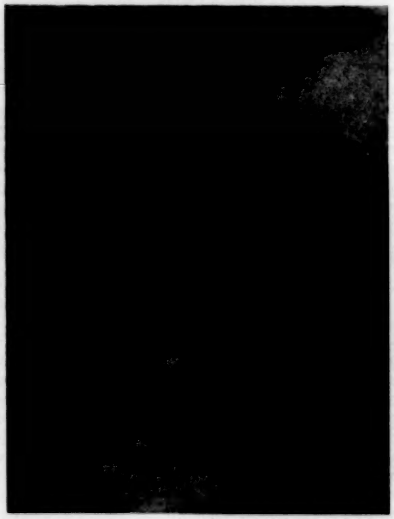

FIGURE 1. *Spot Film of Duodenal Loop Showing Pressure Defect on Its Medial Aspect.*

The blood pressure was 156 systolic, 90 diastolic.

Urinalysis was negative. Examination of the blood revealed a hemoglobin of 14 gm. and a white-cell count of 14,100, with 80 per cent neutrophils and 20 per cent lymphocytes. Two stools were guaiac negative. The nonprotein nitrogen was 22 mg. and the total protein 6.6 gm., with an albumin-globulin ratio of 1.8, the cholesterol 188 mg., the serum amylase 34 units and the total serum bilirubin 0.8 mg. per 100 cc. and the lipase 1.3 cc. The prothrombin time was within normal limits. The cephalin-flocculation test was negative in twenty-four and forty-eight hours. An electrocardiogram showed normal rhythm at 105 with occasional ventricular premature beats. The ST segment was depressed in Lead 1, slightly depressed in Lead V_6, sagging in Leads 2 and AVF and elevated in Lead AVR; the T waves were inverted in Lead 3, low in Lead AVF and slightly depressed in Lead V_4. Cytologic examination of the sputum was doubtful for malignant cells.

Plain x-ray films of the abdomen showed that the liver was probably slightly enlarged, but no splenic enlargement was seen. The renal outlines, bone density and bowel pattern were not unusual. There was a 1-cm. density in the right abdomen that resembled a calcified lymph node. A barium-enema examination and intravenous pyelogram were unremarkable. Gall-bladder series on the third and seventh hospital days failed to show any concentration of dye. A gastrointestinal series showed some distortion of the duodenal loop (Fig. 1). X-ray films of the chest showed some deformity of the right side of the thorax that might have been either congenital or traumatic (Fig. 2). The pulmonary vessels were prominent throughout, in some areas extending well out into the periphery. The right paratracheal, interlobar and hilar lymph nodes were enlarged, as were the left-interlobar and superior-root nodes. The pleura appeared thickened in the right chest posteriorly.

FIGURE 2. *X-ray Film of Chest.*

On the second hospital day the temperature, which had been normal on admission, rose to 102°F. and the white-cell count to 16,500. The patient con-

tinued to have intense pain, and a re-examination of the abdomen showed direct tenderness just to the right of the umbilicus with rebound tenderness in all quadrants. Rectal examination was negative. That evening the pain was most severe in the right upper quadrant, where it was associated with spasm. Both right-costal-margin and costovertebral-angle tenderness could be demonstrated. On the third day the white-cell count reached 31,600, gradually declining to normal over the next week. The temperature remained elevated for five days and then became normal by lysis, without specific therapy. The pain subsided concomitantly.

The maintenance dose of 0.1 mg. of digitoxin was continued throughout the hospital course. An electrocardiogram taken on the third day showed a normal rhythm at 100. The ST segments in Leads AVR and V_1 had become isoelectric and remained depressed in Lead V_4. The T waves had decreased in amplitude in Leads V_2, V_3 and V_4. On the ninth day the patient was started on 0.8 gm. of quinidine sulfate per day, and he received Mercuhydrin injections on the second, tenth, thirteenth and seventeenth days. The occasional extrasystoles disappeared soon after admission, and blood pressure was well maintained throughout the course.

On the eleventh day fluoroscopy disclosed some limitation of motion in the right leaf of the diaphragm. A grid film with barium in the esophagus showed no definite evidence of bifurcation-lymph-node enlargement. A definite primary tumor within the chest could not be identified, but a repeated cytologic examination of the sputum was still doubtful for malignant cells. A review at this time of films taken four and five years previously showed linear densities and hilar enlargement similar to that seen in the admission films of the chest.

A third electrocardiogram taken on the twelfth hospital day showed normal rhythm at 90 and a normal voltage and axis. Since the second record was taken, the T waves in Lead V_1 had become inverted and those in Leads V_2, V_3 and V_4 had become diphasic. The ST segments were isoelectric.

On the seventeenth hospital day an operation was performed.

Differential Diagnosis

Dr. Earle M. Chapman*: I think this case is one of the most puzzling and intricate cases I have ever been invited to discuss in these meetings.

Unfortunately there was no comment on the presence or absence of edema. I assume it was present because of the Mercuhydrin injection.

I should like to start with a review of the x-ray films to see if they will help me more than the description in the text.

Dr. Stanley M. Wyman: The films of the chest show the deformity of the right upper thorax, which I think is probably the result of old injury. There are very fine patchy densities scattered through both lung fields, almost a miliary process. There are, in addition, these rather distinct lobulated soft-tissue masses, particularly in the right paratracheal and right hilar regions, and to a lesser degree on the left (Fig. 2).

Dr. Chapman: Would you call those star-shaped, scalloped or rounded?

Dr. Wyman: I would call them rounded nodular affairs. The barium in the esophagus does not outline any definite masses at the bifurcation of the trachea. The heart shadow is quite prominent toward the left in the region of the left ventricle, but otherwise I can say very little about it. This film was taken with the patient lying on his back; I think there is a great deal of magnification of the heart shadow so that the heart is not as big as it appears here. The plain film of the abdomen shows the visceral outlines very well. The kidneys are not grossly remarkable. The single film from the barium-enema examination shows no definite abnormality. The kidneys are again seen — perhaps a little better — on the pyelogram; they appear normal. There is some gall-bladder dye in the stomach at this time, and a number of films, taken in an attempt to show the gall bladder, show no filling that I can demonstrate.

Dr. Chapman: Where is the calcified area?

Dr. Wyman: I think that is down below here — this little shadow, which I take to be a small mesenteric lymph node. Some of the most interesting films are those of the duodenum, where there is a fairly conspicuous deformity of the second portion (Fig. 1). There seems to be some compression of the medial aspect of the second portion of the duodenum, with a suggestion of some protrusion of the lumen at that point, but I can make no further statement on that. The mucosa seems stretched on this particular film, as though the bowel were enfolding something.

Dr. Chapman: Something located on the medial aspect of the duodenum?

Dr. Wyman: On the medial aspect near the head of the pancreas. The duodenal loop itself is of normal size. It is not the classical stretched-out enlarged duodenal loop associated with an enlarged head of the pancreas. There is a fair amount of scoliosis of the spine, but I think it is probably not pertinent to the problem today.

Dr. Reed Harwood: Have you a good view of the dorsal spine?

Dr. Wyman: No; we do not have one.

Dr. Chapman: Would you comment again on the film that shows some protrusion in the second portion of the duodenum along the inner margin?

Dr. Wyman: In the films available there seems to be pressure on the medial aspect of the second portion of the duodenum over a distance of 3 cm., as though there was something indenting the duodenal loop at that point. The mucosal folds in that portion seem a little stretched, as though from pressure.

*Associate physician, Massachusetts General Hospital.

DR. CHAPMAN: Is there no evidence of ulceration within the duodenum?

DR. WYMAN: I do not see any frank ulceration.

DR. CHAPMAN: May I ask about this fine mottled density throughout the lung fields? Is that consistent with a pneumoconiosis or pulmonary infectious disease?

DR. WYMAN: It is consistent with miliary tuberculosis, with beryllium pneumoconiosis and with sarcoidosis. I think Dr. King[1] has compiled a list of about 50 possible causes of it. I do wish we had the films that were said to have been essentially the same four or five years ago, as that is a most important point.

DR. CHAPMAN: Evidently the medial end of the clavicle is dislocated. Is that true?

DR. WYMAN: It is not that it is dislocated but that the sternoclavicular joint arises here, and the entire chest is twisted toward the right because of the chest deformity.

DR. CHAPMAN: This history did not tell me his occupation. Is there any chance of knowing the occupation?

DR. TRACY B. MALLORY: He drove what is euphemistically termed the "ambulance" for a funeral director.

DR. CHAPMAN: That is a hazardous job! I suppose his previous occupational record is not known.

That is not the picture of pneumoconiosis, as the process extends from the top to the very bottom of the lung fields. In pneumoconiosis the picture so often is fan-shaped, leaving the top and bottom free. Isn't that so?

DR. WYMAN: That is the classical picture in sarcoidosis, for example.

DR. CHAPMAN: After seeing the films, I have to change the opinions I formed in reading the history. I shall take up the problem by steps.

It has always been a clinical maxim to try to fit the whole chain of evidence into one diagnosis whenever possible. This patient had had the signs and symptoms of disease above the diaphragm and then suddenly came into the hospital with disease localized below the diaphragm. I shall first discuss the disease in the chest.

From the physical examination it seems clear that I am dealing with pulmonary hypertension. What are the causes of pulmonary hypertension? There are three or four that I shall have to consider. A chest deformity, kyphoscoliosis, with severe compression of the lungs resulting in a lowered vital capacity, can cause this difficulty. However, the degree of deformity shown in the x-ray films excludes that as the cause of the pulmonary hypertension. Mitral stenosis is a very common cause of pulmonary hypertension and may be missed on auscultation. The description of the murmur was that of a systolic murmur. There was a history of paroxysmal pain that went back over a three- or four-year period, which might well have been angina. However, angina with rheumatic heart disease, especially pure mitral stenosis, is exceedingly rare. Dr. Paul D. White[2] quotes three cases of patients with pure mitral disease and angina who showed at autopsy no evidence of coronary sclerosis to explain the angina. It was thought that the angina was based on the failure to deliver an adequate blood flow through the aortic valve down into the coronary circulation. In the case under discussion there was no x-ray appearance or physical findings to suggest rheumatic heart disease. I think I can exclude mitral stenosis as a possibility.

Another consideration is intrinsic pulmonary disease; one form of this could be diffuse pulmonary endarteritis, a vascular disease producing the so-called black cardiac, — Ayerza's disease, — but this man was not cyanotic; he was merely described as being florid. I think I can exclude that possibility.

The x-ray films obviously showed pulmonary disease. With these x-ray findings, — even without the so-called star-shaped hilar nodes, — one has to consider sarcoidosis. Another possibility is pneumoconiosis acquired from a previous occupation. I think the patient had intrinsic pulmonary disease and pulmonary hypertension, which explained the continued dyspnea and orthopnea, and that along with them he must have had chronic congestive failure — congestion within the lungs and liver, and edema of the ankles. In addition, I am going to assume that the failure of the gall bladder to fill with dye may have been related to the congestion of the liver and its failure to deliver the dye to the gall bladder. I think the finding of questionable malignant cells can be explained on the basis of congestive failure and chronic, nonmalignant pulmonary disease. In such conditions we have seen abnormal cells that simulated those of malignant disease. I do not believe the finding is evidence for malignant pulmonary disease.

The next things I shall consider are the disease processes below the diaphragm and the reason for operation. The signs and symptoms would lead one first to suspect the presence of an acute cholecystitis. I know the physicians must have searched for that condition, but somehow I cannot believe the patient had an acute gall-bladder disease. It is true that acute cholecystitis will change the electrocardiographic pattern, even to the point where it simulates myocardial infarction; by the time of this third tracing, however, the changes had reverted toward normal, so that they were not diagnostic of myocardial infarction but perhaps more in keeping with an acute vascular disease within the abdomen.

Among the possibilities are mesenteric thrombosis, abdominal hemorrhage, a tear in the intima or plugging of a vessel by an embolus. If it was due to emboli, they would be related to the heart, which would have been harboring thrombi and shooting off emboli. A perforated viscus may produce pain that is interpreted as angina and that may even be relieved by nitroglycerin. Since we know that pain due to an ulcer or to gall-bladder disease may be re-

lieved by nitroglycerin, that fact does not differentiate the diagnosis. The patient could have had a duodenal ulcer that perforated, but the radiologist said that there was no evidence of an ulcer in the x-ray film, so I cannot plead for that diagnosis.

From the x-ray evidence it seems that the mass lay outside the duodenum in the region of the pancreas. The findings are consistent with an acute hemorrhagic pancreatitis — a sudden vascular crisis. That could cause the severe pain, the sweating and the apprehension. The distribution of the pain across the abdomen was that of the pain of pancreatitis. Acute hemorrhagic pancreatitis could give rise to a mass that would press on that portion of the duodenum, and I think that is the most likely condition below the diaphragm.

It is possible to relate the abdominal condition to the disease in the chest. He may have had in the abdomen a nodule of the same process that was in the chest that had become necrotic or had had a sudden hemorrhage into it. Although I have never before encountered such a complication of sarcoid disease, I think I must consider the possibility of sarcoid lymph nodes within the abdomen. The flecks of calcification in the pelvis may have been due to a long-healing sarcoid process in a lymph node. It is possible that a sarcoid node had become necrotic from hemorrhage or infarction within it; this would explain the abdominal pain.

This is indeed a puzzling case. I should like to make one diagnosis that would cover the whole situation, but I do not see how I can. I think the most likely diagnosis is long-standing sarcoidosis that had impaired respiratory exchange and caused the symptoms of pulmonary hypertension. I am uncertain about the nature of the acute process in the abdomen, but I suppose it may have been pancreatitis or a necrotic lymph node of the same type that was seen in the lungs. I doubt, on the basis of the electrocardiographic evidence, that the patient had a myocardial infarction.

Dr. Jacob Lerman: I wonder if one should consider a ruptured gall bladder.

Dr. Chapman: If the gall bladder ruptures, does it drain down into that area, Dr. Wyman?

Dr. Wyman: I do not believe I can answer that as well as Dr. Welch, but I do not believe so.

Dr. Claude E. Welch: I think it would be a very peculiar course of events for a man with a perforated gall bladder to recover as well as this patient did. Then, too, the deformity in the duodenum from a perforated gall bladder would be on the outer side of the duodenum, whereas this deformity was on the inner side and suggested something going on in the head of the pancreas rather than in the gall bladder.

Dr. Harwood: It does not look like a surgical emergency such as a perforated ulcer, acute gallbladder disease or an acute pancreatitis.

Dr. Mallory: I cannot subscribe to Dr. Chapman's theory of necrosis and hemorrhage within a sarcoid node. The most characteristic feature of sarcoid lesions besides the miliary tuberculoid foci is the absence of necrosis.

A Physician: How often is the lipase normal with an acute pancreatitis?

Dr. Welch: It occurs occasionally, just as a normal amylase does. It is unusual, however, if the blood is taken within the first twenty-four hours after the onset.

A Physician: I should like to ask Dr. Wyman whether the changes in the lung could be on the basis of chronic pulmonary infection.

Dr. Wyman: Of what sort?

A Physician: He had five episodes of pneumonia.

Dr. Wyman: I do not think the apparent enlargement of nodes or the fine miliary pattern would be nearly so likely with a story like that. One thing that I would have to add as a possibility is lymphatic spread of cancer. We could not exclude that from the x-ray point of view.

Dr. Chapman: Yes; after seeing the films with the fine spread of what could well have been cancer, I had considered the possibility of a carcinoma of the gall bladder with metastases and distortion of the duodenum. However, with the symptoms of dyspnea, a cough present for four years and recurrent infections, I do not see how that could have been cancer.

Dr. Walter St. Goar: What about some other disease such as cysts or fibrosis?

Dr. Chapman: One thinks perhaps of that disease in a child; quite often they have congenital cystic pancreatitis and bronchiectasis, but they rarely live to be adults. The x-ray films of the chest are not those of that type of disease.

Dr. Wyman: Those children do not live beyond their teens, so far as I know.

Dr. St. Goar: I think adults do have cystic disease of the pancreas, not unlike the children's disease.

Dr. Mallory: The cysts seen in adults are quite different in character. Some are neoplastic and usually are single, relatively large masses. There are also retention cysts due to plugging of the ducts, but only one or two cysts are present. Fibrosis is unusual, and the condition is not progressive. Still another lesion occurs in adults, which has been called ectasia of pancreatic ductules and acini. Baggenstoss[3] found it particularly frequently in association with renal insufficiency, and I saw it very frequently during the war, especially in patients with typhus. The cysts are always microscopic and there is no fibrosis.

Dr. Chapman: I suppose one might classify this man's type of failure, which had been going on for many years, as pulmonocardiac failure, the chest disease — whatever it was — causing fibrosis and pulmonary hypertension. He must have had a

very low vital capacity. There was no record of its being tested, was there, Dr. Mallory?

DR. MALLORY: Not to my knowledge.

CLINICAL DIAGNOSES

Cholecystitis.
Coronary heart disease.
?Pulmonary sarcoidosis.
?Pulmonary metastases from tumor of unknown origin.

DR. CHAPMAN'S DIAGNOSES

?Acute pancreatitis. ?Necrotic abdominal sarcoid lymph node.
Pulmonary hypertension; intrinsic pulmonary disease — ?sarcoidosis.
Congestive heart failure.

ANATOMICAL DIAGNOSES

Gangrenous cholecytitis with localized perforation.
Cardiac hypertrophy, right ventricle.
Coronary sclerosis, severe, with myocardial fibrosis of right ventricle.
Pulmonary emphysema and fibrosis, moderate.
Chronic passive congestion of lungs.
Kyphoscoliosis.

PATHOLOGICAL DISCUSSION

DR. MALLORY: Laparotomy was done on this patient and an inflamed gall bladder was found, with a localized, well walled off perforation. A portion of the wall of the gall bladder was described as being gangrenous. It was removed, and the patient died within a few hours after operation without any very distinctive signs or symptoms.

Autopsy showed that he did have severe arteriosclerotic heart disease with marked atheromatous narrowing of all the coronary arteries but without any definite area of infarction. The right heart was rather unusually thick, the right ventricle measuring 7 mm., approximately twice the normal thickness. Microscopical sections of the myocardium showed rather extensive fibrosis in the right ventricle and comparatively little in the left ventricle. That is an unusual sequel of coronary sclerosis. It is quite common to find patchy fibrosis of the left ventricle in a patient with severe coronary disease with little or no involvement of the right side. In this case the usual pattern was reversed. Very large atheromatous plaques with a little calcification were found on the aortic and mitral valves, but neither valve showed enough deformity to be described as stenotic.

The mediastinal lymph nodes were somewhat enlarged but not very impressive on microscopical examination. There was some nonspecific lymphoid hyperplasia and a moderate but not very severe degree of anthracosis. There was no evidence of sarcoidosis or of any type of pneumoconiosis. I do not believe the carbon pigment itself would account for the findings. Grossly the lungs were not remarkable; microscopically there was some chronic passive congestion, moderate emphysema and fibrosis, and intimal thickening of the pulmonary arteries.

The pancreas showed a severe grade of postmortem degeneration, but I think that any antemortem pancreatitis can be safely excluded. The calcified mesenteric lymph node was found to explain the small shadow visualized in the x-ray films just medial to the iliac crest.

DR. CHAPMAN: I think it is extraordinary that this degree of pulmonary congestion was on the basis of a long-standing coronary heart disease with production of a syndrome of pulmonary hypertension from failure — chiefly, perhaps, in the right ventricle. Could this fibrosis have weakened the wall of the right ventricle and caused back pressure within the pulmonary system, chronic pulmonary congestion through the whole lung field simulating pneumoconiosis, or sarcoidosis, with drainage back to the lymph nodes?

DR. MALLORY: I do not believe we have a good explanation for the pulmonary hypertension in this patient. Certainly the mitral valve did not explain it. Perhaps the combination of fibrosis, emphysema, kyphoscoliosis and pulmonary arteriosclerosis was enough to account for it.

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CASE 37222

PRESENTATION OF CASE

A sixty-two-year-old woman entered the hospital because of headaches, confusion, and incontinence.

The patient was well until about three weeks before admission, when she developed sudden severe pain in the right eye and orbital region "as if a nail were being driven into my eye." This pain persisted for some four days, subsided and then recurred with less intensity than at first. Approximately simultaneously with the onset of the headaches, her family and her physician noticed that she had become confused as to time — she forgot to prepare meals on time, burned the food and forgot appointments. Impairment of memory for recent events in general and some confusion about familiar geographical relations were likewise observed. Shortly after this she began to have urinary (and, rarely, fecal) incontinence. At about the same time, drooping of the left corner of her mouth was observed.

In the past she had been an active, intelligent woman, with good general health. In childhood she had pulmonary tuberculosis with complete recovery. About twenty-five years before entry she had a duodenal ulcer, which had been asymptomatic for years on dietary management. For several

months before the present illness she had complained of left-costovertebral-angle pain, and pus had been found in the urine. Urine cultures and guinea-pig inoculation tests made elsewhere were negative. The past and family histories were otherwise not remarkable.

On examination the patient was garrulous and facetious. Speech was clear and coherent, but she was vague as to details of her history and did not follow simple instructions well. On neurologic examination the fundi, confrontation fields, pupils and ocular movements were normal. There was left-facial weakness. The palate and tongue were normal. Motor functions were normal in the arms and in the right leg. There was slight weakness of left-hip flexion, but muscle tone in the left leg was normal. Tendon reflexes were active and approximately equal, although some examiners thought that the knee and ankle jerks were a little more active on the right. The abdominal reflexes were less active on the left. The right plantar reflex was normal, the left doubtful. Sensation was normal throughout. The general physical examination was not remarkable.

Examination of the blood revealed a hemoglobin of 13.4 gm. and a white-cell count of 11,100, with 67 per cent neutrophils. A catheterized urine specimen had a specific gravity of 1.005 and gave a + test for albumin and a negative test for sugar; the sediment contained occasional white-cell clumps. Cultures were negative. The blood sedimentation rate was 9 mm. in one hour. The blood nonprotein nitrogen was 31 mg. per 100 cc. A stool was guaiac negative. An electrocardiogram was not remarkable. An electroencephalogram gave an abnormal record characterized chiefly by slow high-voltage activity, most marked in the left frontal region but present also in the right frontotemporal region. On lumbar puncture the cerebrospinal fluid was clear, colorless and under an initial pressure equivalent to 210 mm. of water. The fluid contained no cells and a total protein of 138 mg. per 100 cc.; the gold sol was 0001222100.

X-ray films of the skull were not remarkable. The clinoid processes were not eroded. An x-ray film of the chest showed no abnormality in the lungs, but there was enlargement of the heart shadow in the region of the left ventricle. A gastrointestinal series demonstrated deformity and narrowing of the duodenal cap but no visible crater, and there was retention of about one half of the barium meal in the stomach after six hours. The duodenal loop appeared normal. Films of the spine showed extensive osteoporosis. Intravenous pyelograms were not entirely satisfactory but showed no abnormalities.

On the ward, the patient's mental status was variable. She was consistently alert and responsive, but at the same time she was to a greater or lesser degree disoriented and confused. As time passed, this confusion became more marked and was accompanied by intermittent lethargy and apathy. At first, she complained from time to time of frontal and right-orbital headache, but after several days the headaches subsided. She was repeatedly incontinent of urine. A neurologic examination about two weeks after admission showed persistent left-facial weakness but no definite abnormalities in motor performance of the limbs (except for nonspecific unsteadiness of gait), sensations or reflexes.

On the nineteenth hospital day an operation was performed.

Differential Diagnosis

Dr. Vincent P. Perlo*: The triad of headache, mental confusion and increased spinal-fluid pressure indicates that the patient had a space-occupying intracranial lesion, and, on the basis of the short history, a rapidly progressive one. Before attempting to decide about the diagnosis, I should first like to try on the basis of the clinical data to localize the part of the brain involved. The patient's first symptom was severe right-sided headache localized behind and above the right eye. This has an important localizing value in a patient with a space-occupying intracranial lesion. Since the headache was quite severe, one thinks first of the possibility of irritation of the subarachnoid space in the frontal region, perhaps due to blood in the spinal fluid. Also one thinks of direct involvement of the first branch of the trigeminal nerve. The patient did not have any disturbance of consciousness at the time the headache came on, and she had no stiff neck, nausea or vomiting, so I can be fairly sure that there was no bleeding into the subarachnoid space. On admission to the hospital the cranial nerves were normal, which indicated that there was no direct involvement of the trigeminal nerve on the right side. I assume that the headache points to an intracerebral lesion behind the eye in the right frontal region and was probably caused by distention of the meninges and meningeal vessels.

The next important symptoms that occurred at about the same time as the headache were memory impairment of a severe degree, confusion, disorientation and, within three weeks, evidence of marked personality deterioration. She was described on admission as being garrulous and facetious and quite unlike her former self. It is important to note that at the time she had these mental changes she was alert and responsive and remained so for a few days after admission. The finding of such mental symptoms in a patient who is alert is fairly reliable evidence of frontal-lobe involvement on the dominant side. If a patient has such mental symptoms but at the same time is lethargic and apathetic, one cannot be sure that they are not due to generalized increased intracranial pressure. How-

*Assistant in neurology, Massachusetts General Hospital.

ever, in this case the intracranial pressure was only slightly elevated, and in view of the patient's alertness I accept the mental symptoms as dominant frontal-lobe signs. She was incontinent shortly after the illness started and continued so. The incontinence must represent a lack of higher cortical control over the bladder and anal reflexes; it is quite commonly seen in frontal-lobe lesions.

I should like to ask whether the patient was right- or left-handed?

DR. CHARLES S. KUBIK: Right-handed.

DR. PERLO: Since the patient was right-handed, that makes it somewhat difficult, because I have to assume that the left frontal lobe had to be involved to cause the disorder in personality, although the headache indicated involvement on the right side and there were important objective neurologic findings that also suggested involvement of the right frontal lobe. The patient had left-facial weakness. This is a reliable sign of upper motor neurone involvement just anterior to the motor region in the right prefrontal area. She also had some weakness in the left lower extremity, albeit slight. The left plantar response on admission was doubtful as compared with a normal right plantar response. The abdominal reflexes on the left side were slightly less active than those on the right. There are suggestive signs of pyramidal-tract involvement, pointing to a lesion within the right frontal lobe.

Except for the findings I have mentioned, the remainder of the neurologic examination was normal. That tells me that the remaining areas of the brain were functioning normally and could not have been involved. There was no involvement of the cranial nerves. This leads me to believe that the lesion or lesions must have been intracerebral, were not exerting pressure on the brain from the outside and were localized fairly definitely to both frontal lobes. The spinal-fluid examination was of importance. The increased cerebrospinal-fluid protein reflects involvement of the brain close to the subarachnoid space or close to the ventricular system and is not specific except that it suggests intracranial tumor. The initial pressure was 210 mm., slightly above the upper limit of normal of 200 mm., so there was a slight degree of increased intracranial pressure. At the same time the mental symptoms were severe, and one can be sure they were not caused solely by increased intracranial pressure. Again, this points to an invasive lesion of the frontal lobes. The electroencephalogram was of interest; it showed high-voltage slow-wave activity over both frontal lobes, more marked on the left side. Such a finding in an electroencephalogram is not specific, although it is very suggestive of a space-occupying lesion in the frontal region, probably more on the left side — if I can accept the electroencephalographic localization. The electroencephalographic finding of more abnormality of the left side goes along with the clinical observation that the patient's dominant hemisphere must have been involved. I am satisfied that the patient probably had infiltrating intracerebral lesions in both frontal lobes.

I wonder if I might see the x-ray films to see if there is any additional clue?

DR. JAMES J. MCCORT: I have very little to add to what has been stated in the protocol. The bones of the skull are quite normal. The sella turcica shows no evidence of erosion. The posterior clinoids are well seen and do not appear to be destroyed. There is possibly slight calcification in the region of the carotid artery. There is no evidence of bone erosion or any abnormal intracranial calcification.

DR. PERLO: Can the pineal be seen?

DR. MCCORT: No; it is insufficiently calcified for localization.

The chest is entirely negative. On the intravenous pyelogram no gross change can be demonstrated in either urinary tract and the kidneys are not enlarged or displaced. The gastrointestinal tract is of some interest. In the stomach the rugal folds are somewhat wide and coarse, but we know that the stomach was pliable, and in the films there is no evidence of tumor. The duodenal cap is constricted because of scarring from the previous duodenal ulcer. A barium-enema examination is negative.

DR. PERLO: I expected that the x-ray films of the stomach would give me an important lead, but I am somewhat disappointed.

There are several conditions to be considered in the differential diagnosis of a rapidly developing, expanding frontal lesion in a sixty-two-year-old woman. First, one must consider the possibility of a primary intracerebral hemorrhage that occurred at the time of the severe headache and then manifested itself as a space-occupying encapsulated lesion in the right frontal lobe. However, the fact that the patient did not lose consciousness at the onset is, I believe, enough evidence to rule out a primary intracerebral hemorrhage. In addition, the fact that she did not develop any weakness of the opposite side at the onset makes me doubly certain that it was not this type of cerebrovascular disease. One has to consider briefly the possibility of an aneurysm of the internal carotid artery that ruptured mainly into the brain substance, giving the very same picture as an intracerebral hemorrhage. For the same reasons that hemorrhage was ruled out I think ruptured aneurysm can be excluded. Moreover, there was no evidence of bleeding into the subarachnoid space; subarachnoid bleeding occurs in most cases of ruptured aneurysm.

The next possibility is brain abscess. Occasionally brain abscess cannot be distinguished clinically from tumor, and at times one is discovered quite by accident during an intracranial operation for tumor. This patient had a history of some left-costophrenic-

angle pain and some evidence of inflammatory disease involving the left kidney; that was a possible focus of infection. Against intracerebral abscess are the following: The patient did not have any systemic signs of infection, the white-cell count and sedimentation rate were normal and the spinal fluid did not show any cells; for those reasons I think I can rule out abscess fairly definitely. Tuberculoma, which also may act as a space-occupying lesion, may be mentioned in passing as a remote possibility. The patient had a history of tuberculosis many years before admission. However, there was no evidence of any recent tuberculous activity. A tuberculoma would produce some systemic manifestation of infection — and cells in the spinal fluid.

In a patient who presents rapidly progressive deterioration and signs of increased intracranial pressure, one must consider the diagnosis of subdural hematoma. There was no history of injury, but in approximately 50 per cent of cases of subdural hematoma no history of injury is obtained. What is there against subdural hematoma in this case besides the fact that there was no injury? I believe the symptoms are to be explained on the basis of an infiltrating lesion of the frontal lobe, for the reasons I have already given, and a subdural hematoma would manifest itself by compressing the brain from the outside. It would be most unusual for a patient going downhill from a frontal subdural hematoma not to show fairly definite lateralizing findings by the time the mental status became severely impaired. The spinal-fluid protein is usually not so high in subdural hematoma as it was in this case. The fact remains that once the question of a subdural hematoma is raised it may be impossible to rule it out entirely except by operation.

I believe that the patient must have had a brain tumor. I have already committed myself to involvement of both frontal lobes on the basis of the facts that the headache was more pronounced on the right side and that the patient had neurologic signs indicating a right-frontal lesion and also some evidence of left-frontal involvement. The clinical course of rapidly developing symptoms over a period of less than a month enables me to rule out a slowly growing tumor, such as meningioma, astrocytoma or oligodendroglioma. The normal skull films indicate that whatever was wrong inside the patient's head had not been going on for a long time. There was no evidence in the x-ray films of increased intracranial pressure and no evidence of the calcification that one might expect from a slowly growing neoplasm.

One primary brain tumor that could account for the patient's symptoms would be a glioblastoma multiforme, a rapidly growing, malignant, invasive tumor that at times can run its course in a matter of a few weeks, although usually the history goes on for a period of months or longer. Also parallel with the possibility of glioblastoma multiforme is the diagnosis of metastatic tumor. In order to make the latter diagnosis, it would be important to find the site of the primary lesion. Moreover, it would be most unusual to have metastatic disease of the brain without having involvement of the chest first, — although that is not invariably the rule. At times a metastatic tumor is found at operation or at autopsy, having completely simulated a primary brain tumor, with the primary source of the lesion being entirely overlooked.

Can I explain the involvement of the right frontal lobe and left frontal lobe on the basis of a glioblastoma multiforme? Occasionally gliomas extend across the midline by way of the corpus callosum and involve both frontal lobes. That is a possibility in this case. The clinical features are so typical of metastatic carcinoma of the brain that I hesitate to give up that diagnosis, but I think I shall have to do so in view of the fact that the stomach lesion was definitely not a malignant one and there was no evidence of kidney tumor. I am left with a diagnosis of glioblastoma multiforme involving mainly the left frontal lobe and extending across the corpus callosum to involve the right frontal lobe also. I think the patient also had chronic pyelonephritis on the left and probably scarring of the duodenum secondary to the ulcer twenty-five years previously.

Clinical Diagnosis

Tumor, right frontal lobe.

Dr. Perlo's Diagnoses

Glioblastoma multiforme, left and right frontal lobes.
Chronic pyelonephritis.
Scarring of the duodenum secondary to healed ulcer.

Anatomical Diagnosis

Glioblastoma multiforme, right frontal lobe.

Pathological Discussion

Dr. Charles S. Kubik; The operation mentioned in the clinical account was an arteriogram. Perhaps Dr. McCort will show us the films.

Dr. McCort: A right-cerebral arteriogram was performed. The films disclosed displacement of the right anterior cerebral artery to the left side (Fig. 1). The middle cerebral artery is displaced slightly posteriorly and slightly downward, and the carotid artery syphon is displaced slightly (Fig. 2). There is, in the region of the maximal displacement of the anterior cerebral artery, a suggestion of a cluster of tiny capillaries that represent the so-called tumor stain.

Dr. Kubik: I might say that we were puzzled because of the sudden onset of symptoms and by the conflicting evidence of pain over the right eye with the electroencephalogram suggesting a lesion of the left side. Dr. Selverstone carried out his

examination with radioactive potassium and found indications of a tumor in the form of a greatly increased Geiger count over the right frontal region, and these indications were confirmed by the arteriogram, as you have heard.

Dr. William H. Sweet then explored the right frontal region and found on the surface of the brain

FIGURE 1. *Arrows Point to Left-sided Displacement of the Right Anterior Cerebral Artery.*

near the frontal pole a discrete tumor, 5 or 6 cm. in diameter, which proved on frozen-section examination to be glioblastoma multiforme. He removed what both he and I thought was all the tumor, together with a large portion of the frontal lobe, remaining well in front of the motor cortex, which was identified by electrical stimulation; the opposite hemisphere apparently was not involved. When the specimen itself was examined after it had been removed it seemed to us that the excision had been made too close to the tumor and, since the tumor was so discrete and might conceivably be successfully removed, we thought that the removal of more brain tissue would be advisable. That was done, and the patient got along fairly well until three days after operation, when she developed a stitch infection and a subsequent meningitis, for which she is being treated now.

Although it seemed that the motor cortex had been avoided by a safe margin, the first operation was followed by a severe left hemiplegia, which improved very little. The mental status was very little different from what it had been before the operation. After the second operation there was very little change in the patient's condition until after she developed meningitis.

This type of tumor, as you know, is almost never or perhaps never cured. In post-mortem material

FIGURE 2. *Arrows Point to Frontal Tumor and to Slight Posterior Displacement of the Middle Cerebral Artery.*

tumor cells are found a considerable distance beyond grossly visible tumor and sometimes invade almost the entire hemisphere. However, in at least one case that came to post-mortem examination several weeks after operation we were unable to find any residual tumor, so there was some reason for supposing that successful removal might have been possible.

The New England Journal of Medicine

Formerly
The Boston Medical and Surgical Journal
Established 1828

Official Organ of
THE MASSACHUSETTS MEDICAL SOCIETY
and
THE NEW HAMPSHIRE MEDICAL SOCIETY
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Microfilm volumes available to regular subscribers through University Microfilms, 313 N. First Street, Ann Arbor, Michigan.

Material, other than original articles, should be received not later than noon on Thursday, three weeks before date of publication.

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Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts. Telephone KE 6-2094.

TWENTY-TWO FENWAY

THE officers of the Massachusetts Medical Society moved into their new quarters at 22 Fenway on April 23; on May 22, during the course of the annual meeting of the Society, a reception was held at which an opportunity was given to fellows and their families to inspect the premises. This event was the informal opening of the Society's home; a more formal dedication is planned for some future date.

This substantial and, it is hoped, relatively permanent establishment of the Society represents a decided departure from the situation that existed scarcely more than a decade ago. Then all the headquarters company that the Society had available consisted of the executive secretary and the *Journal* office force, giving part-time services, who were sporadically visited by the elected officers.

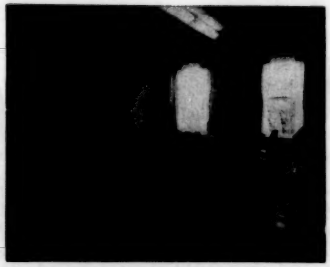
As the Society has increasingly concerned itself with socio-economic, legislative and educational matters and with public relations in general, the staff has rapidly increased to the point where the secretary and executive secretary, the director of medical education and information and his assistant, and a force of four office secretaries and a telephone operator and receptionist are on a full-time basis, the treasurer and assistant treasurer continuing on part-time salaries.

The activities of this group have seemed to justify its existence. As He that keepeth Israel shall neither slumber nor sleep, so those that direct the functions of the Massachusetts Medical Society and help to maintain its integrity in the service of the public are accustomed to practice eternal vigilance in the discharge of their duties.

The building that now houses the Society, once one of Boston's most imposing residences, erected in firm juxtaposition to the Medical Library as if symbolic of their mutually indispensable relations, has undergone a series of major plastic operations to fit it for its new purposes. The fourth floor, originally only a half portion, has been extended to the front of the building, where great windows look out over the Fenway. Here the director of medical information and education and his assistant plan their work and dream their dreams and brood over the enigmatic future of medicine; in the rear, space has been assigned to the Committee on Postgraduate Education.

The third floor also is given over entirely to offices for the president and secretary, the treasurer, the executive secretary and the clerical staff. On the second floor are committee rooms and a small auditorium that can accommodate some fifty persons; the main floor includes a lounge, a large committee and supper room, impressively paneled in mahogany, and a serving room. Although no rooms are designated for the exclusive occupancy of any persons or committees other than those listed, ample space is available for the use, as needed, of all other committees, the Woman's Auxiliary and the editorial board of the *Journal* for its regular meetings.

Appointed as it is in excellent taste, the building is nevertheless primarily functional in its new role, the ground-floor lounge being the only room set aside for purely social purposes. In such an admirably planned setting the affairs of the Society can be conducted in the most efficient manner for many years to come.

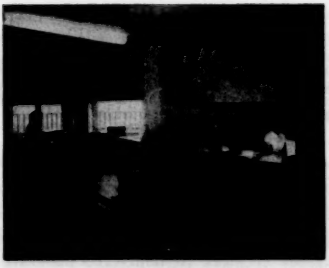


Office of President and Secretary

Director of Medical Information and Education

First Floor Conference Room

Second Floor Conference Room



Secretarial Office

Entrance Hall

SIGNING OF BOOK REVIEWS

THE *Journal* has this spring adopted a minor change in policy, consisting of the signing of book reviews. The change was made not without careful consideration, for it involved the abandonment of a custom of long standing that had been unanimously reaffirmed in recent years by the Committee on Publications of the Massachusetts Medical Society and the editorial board of the *Journal*. The change also was unanimously approved by these same responsible bodies.

Of the four prominent medical weeklies published in English, one on each side of the Atlantic, — the *British Medical Journal* having adopted this policy over three years ago, — now requires the signing of reviews. The *Lancet* and the *Journal of the American Medical Association* still hold to anonymity in this respect.

Much can be said on both sides of this interesting and at times hotly debated question. An anonymous review, according to an editorial printed in the *Journal*[1] in December, 1943, "is likely to be more truly informative than one that is signed or initialled," the inference being that the reviewer may not be honest in his expression of opinion if he knows that his name is to appear in connection with the review.

Greater objectivity and candor are to be expected in the unsigned review, according to its proponents; so, too, is there the danger that liberty may be confused with license and that unjustified criticism may be made without the danger of retribution. "It is one thing to meet one's enemy at the gate," as the editor of the *British Medical Journal*[2] has said, "but quite another to be caught by him in the ambush of anonymity."

It has furthermore been the experience of the *British Medical Journal*, after abandoning the furtive review, "that reviewers, now they put their names to what they write, take much more care than they used to, and, too, they do not hesitate to be critical."[2]

It is to be expected that none of the reviewers for the *New England Journal of Medicine* are so craven as not to write what they believe to be the truth; it is to be hoped that the authors of the books reviewed have their emotions so well in hand that no duels need result if the names of their critics are revealed.

Some person or persons must assume the responsibility for every word that is published in a reputable periodical. The major part of this responsibility is obviously assumed by the writers of original articles and signed communications, although the editors cannot escape a share of the responsibility for having published the material. The responsibility for editorials rests squarely on the editors. So, too, under the system of anonymity, the editor must take the responsibility for book reviews, although he may have not the faintest idea of what some of them are all about. This is a responsibility that should properly be shared by the reviewer.

REFERENCES

1. Editorial. Book reviews. *New Eng. J. Med.* 229:913, 1943.
2. Clegg, H. On signing reviews. *World Med. Assoc. Bull.* 3:15, 1951.

ANTIBIOTICS AND CHEMOTHERAPY

WITH the first issue appearing under this title in April of this year, we welcome the latest addition to the ever growing list of medical periodicals. Heralded as a "Journal of Experimental and Clinical Studies in Antibiotics, Hormones and Chemotherapy," this monthly periodical is published as a private undertaking by the Washington Institute of Medicine. Its editor-in-chief is Dr. Henry Welch, director of the Antibiotic Division of the Food and Drug Administration, and Dr. Felix Marti Ibanez of New York is listed as the "International Editor." To these names has been added an array of 72 others, from among well known contributors in these fields, to constitute the editorial board.

The first issue contains 15 articles covering a wide range of subjects that are encompassed in the scope of the new journal. In addition, there are a few pages of abstracts from other journals and some book reviews.

The tremendous activity in the fields covered by this journal, both in laboratories and in clinics, and the ever increasing numbers of papers being published on these subjects have prompted the courageous sponsors to undertake publication of this new journal at a time when most of the estab-

lished periodicals are having increasing difficulty in sustaining themselves because of mounting costs. It will undoubtedly fulfill a useful need and be in great demand by many workers as an outlet for their publications. It should also attract a large number of readers and prove to be a useful addition to the scientific and clinical journals of our medical libraries.

M. Love, a French naval surgeon, recommends, in the administration of cod-liver oil, that it be combined with a mucilage containing pancreatic juice, which thus forms an artificial chyle. In this form the oil is readily and completely absorbed, and its effect more readily obtained in phthisis.

Boston M. & S. J., *June 4, 1851*

NEW HAMPSHIRE MEDICAL SOCIETY

DEATH

HOPKINS — Arthur W. Hopkins, M.D., of West Swanzey, New Hampshire, died on April 30, 1951, at the home of his daughter, Dr. Faith Baver, in Pennsburg, Pennsylvania. He was in his seventy-fifth year.

Dr. Hopkins was born in Lyndonville, Vermont, the son of Charles H. Hopkins and Ellen J. (Colby) Hopkins. He graduated from Dartmouth College in 1899 and from Dartmouth College Medical School in 1902.

Dr. Hopkins served for over forty years as school and town moderator; he was also health officer and a member of the Swanzey school board. He was a member of the state legislature for two terms. He was a past president of the Cheshire County Medical Society and a member of the New Hampshire State Medical Society, the American Medical Association, the Knights of Pythias, Lincoln Grange, Golden Cross, Red Men and the Federated Church in West Swanzey.

In 1944 he wrote a story of his life as a country physician entitled "Pep, Pills and Politics," a story of a horse and buggy doctor who had graduated to an automobile.

Dr. Hopkins was married to Grace W. Harvey on June 22, 1903. He is survived by his widow and his daughter; a brother, Charles, of Manchester; a nephew, Kenneth Maxfield, of West Swanzey; four grandchildren and several nieces and nephews.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Clinical Uses of Intravenous Procaine. By David J. Graubard, M.D., assistant visiting surgeon, Cumberland Hospital, and assistant visiting orthopedist, Kingston Avenue Hospital, Brooklyn, New York; and Milton C. Peterson, M.D., visiting anesthesiologist, Research Hospital, Kansas City, Missouri. 8°, cloth, 104 pp., with 8 illustrations and 7 tables. Springfield, Illinois: Charles C Thomas, 1950. $2.25. (Publication No. 73, American Lecture Series.)

This monograph presents a study of the literature on the administration of intravenous procaine in various disorders and conditions, including pruritus, serum sickness and sensitivity, burns, postoperative pain, acute arrhythmias, traumatic and inflammatory pain and acute poliomyelitis. The first three chapters deal with history, chemistry and pharmacology, and intravenous administration of local anesthetics. The various chapters have separate lists of references. There is an author index.

Currents in Nutrition: Proceedings of the Nutrition Symposium held at the University of Illinois, College of Medicine, November 19, 1949. By Bertha Burke, William J. Darby, L. Emmett Holt, Jr., M. K. Horwitt, Ancel Keys, Carl V. Moore, James M. Strang and R. W. Vilter. 8°, paper, 128 pp. New York: The National Vitamin Foundation, 1950. $1.00. (Nutrition Monograph Series, No. 2.)

This report presents articles on the thiamin and riboflavin requirements in man, on the B vitamin requirements of infants, pyridoxine deficiency syndrome in man precipitated by a diet low in vitamin B complex and desoxypyridoxine, maternal and other factors of importance to the fetus and mother as shown by dietary histories, the newer hematopoietic vitamins, iron metabolism and hypochromic anemia, the problem of the evaluation of obesity and its significance, and comments on other problems of obesity.

German Aviation Medicine, World War II. Vol. I and II. Prepared under the auspices of the Surgeon General, United States Air Force. 4°, cloth, with illustrations. Vol. I. 648 pp., Vol. II, 654 pp. Washington, D. C.: Superintendent of Documents, United States Government Printing Office, 1950. $4.25. (Vol. I and II, $8.50 [must be purchased in sets].)

The information contained in this comprehensive survey was obtained by the United States Air Forces during the last period of World War II. Special expert teams visited all places where medical research had been carried on by the Germans, and it soon became apparent that a great deal of basic medical aviation research had been carried on throughout Germany during the war. The first volume discusses development and organization of aviation medicine in Germany, aerodynamics, high-altitude studies and acceleration. The second deals with vibration, problems of heat and cold, special senses, the eye, the ear and mechanoreceptors, selection, training and care of the flier, emergency procedures (including air evacuation, air-sea rescue and thirst) and the effects of air warfare on the civilian population. The text is well arranged and well written. The pages are numbered consecutively, and there is a good index. The publishing is excellent. The price is very low, and the set should be in all medical libraries and in all collections on aviation and military medicine.

A Manual of Cerebral Palsy Equipment. 4°, paper, 127 pp. Chicago, Illinois: National Society for Crippled Children and Adults, Incorporated, 1950. $3.75.

This manual lists and illustrates all the standard equipment used by patients in their daily lives and training.

Lehrbuch der gerichtlichen Medizin: Einschliesslich der ärztlichen Rechtskunde ärztlichen Standeskunde sowie der Versicherungsmedizin. By Albert Ponsold, professor of legal medicine, University of Münster. 8°, cloth, 568 pp., with 169 illustrations. Stuttgart: Georg Thieme, 1950. DM 49. $11.65.

This new book is comprehensive in its scope. It is the joint work of seventeen experts in their particular fields. The subjects covered include: the physician and the criminal law, legal psychiatry, causes of death, the determination of paternity, alcoholism, the law and wounds, sexual degeneracy, medical ethics, insurance medicine and expert opinion. There is an extensive chapter on medicolegal methods of analysis. The section on the causes of death is extensive in its scope, covering the whole field from post-mortem appearances to sudden death in the young and old, and takes up more than half the book. The material is well arranged, and the text is written in simple German. There is an index of twenty pages. The publishing is excellent. The book should be in all collections on legal medicine.

Essentials of Medicine: The basis of nursing care. By Charles P. Emerson, Jr., M.D., associate professor of medicine, Boston University School of Medicine, member, Robert Dawson Evans Memorial Laboratory, visiting physician and physician in charge of clinical laboratories, Massachusetts Memorial Hospitals, attending physician, Cushing Veterans Administration Hospital, and medical consultant, American Red Cross; and Jane E. Taylor, R.N., M.Ed., lecturer, Frances Payne Bolton School of Nursing, Western Reserve University. Sixteenth edition. 8°, cloth, 815 pp., with 191 illustrations. Philadelphia: J. B. Lippincott Company, 1950. $4.00.

This manual was first published in 1908. This new edition has been revised and brought up to date. New material comprises preventive medicine, including the chemotherapy of infectious diseases and the pathogenesis of congenital defects; the treatment of neoplastic, infectious, nutritional and allergic disorders; and psychomatic medicine. Naturally, the care of the patient is emphasized throughout the text. The material is well arranged, and there is a good index.

Essentials of Ophthalmology. By Roland I. Pritikin, M.D., eye surgeon, Rockford Memorial, Winnebago County and Swedish-American Hospitals, and consulting ophthalmologist, Saint Anthony Hospital, Rockford, Illinois. 12°, cloth, 361 pp., with 215 illustrations. Philadelphia: J. B. Lippincott Company, 1950. $7.50.

In this manual the author has covered the whole field of ophthalmology. The text is divided into two parts, the first of which includes anatomy, physiology, examination, the extraocular muscles, spectacles and industrial ophthalmology. The second part deals with the diseases of the eye in six chapters arranged in anatomic order. There is a good index, and the book is well published.

Principles of Ophthalmology. By Thomson Henderson, M.D., senior surgeon, Nottingham and Midland Eye Infirmary, and ophthalmic surgeon, Royal Midland Institution for the Blind. 8°, cloth, 230 pp., with 63 illustrations. New York: Grune and Stratton, 1950. $4.50.

The major portion of this book is devoted to the anatomy and physiology of the eye in human beings and mammals, based on a large number of serial sections of eyes in man and animals. There are special clinical chapters on glaucoma and on the corneosclera. The first chapters deal with the mammalian globe, the angle of the anterior chamber, the mechanism of accommodation and the intraocular pressure. The printing, which was done in Great Britain, is excellent.

Cranioplasty. By David L. Reeves, M.D., consultant in neurologic surgery, Santa Barbara Cottage Hospital, Saint Francis Hospital and Santa Barbara General Hospital, Santa Barbara, California. 8°, cloth, 119 pp., with 71 illustrations. Springfield, Illinois: Charles C Thomas, 1950. $3.00.

This monograph is devoted to a comprehensive study of the pertinent literature on cranioplasty. The various types of grafts and operative procedures and other aspects of the operation are discussed. A number of illustrative case histories conclude the text. There is a bibliography of 402 titles of articles. The small book is well published, but the lack of author and subject indexes detracts from its reference value.

Enzymes — Growth and Cancer. By Van R. Potter, Ph.D., professor of oncology, University of Wisconsin Medical School, Madison, Wisconsin. 8°, cloth, 64 pp. Springfield, Illinois: Charles C Thomas, 1950. $1.85. (Publication No. 75, American Lecture Series.)

This monograph constitutes a study of enzyme activity. It is divided into five parts: the role, determination and organization of enzymes, factors influencing enzyme activity, and enzyme inhibition and chemotherapy. The author believes that a cure for cancer may be provided by a prolonged, careful comparison of cancer tissues with normal tissues, for the purpose of ascertaining which enzymes represent the weakest parts of the mechanism that sustains the cancer cell, leading to a discovery for inhibitors of these enzymes. A short bibliography is appended to the text. The lack of a table of contents or an index is noted.

Types of Diabetes Mellitus and Their Treatment. By Arthur R. Colwell, M.D., associate professor of medicine and director of medical specialty training, Northwestern University Medical School, attending physician, Evanston Hospital, and consulting physician, Wesley Memorial Hospital and Municipal Tuberculosis Sanitarium, Chicago. 8°, cloth, 97 pp., with 6 illustrations and 18 tables. Springfield, Illinois: Charles C Thomas, 1950. $2.25. (Publication No. 67, American Lecture Series.)

In this small monograph the author divides diabetes into four classes: unproved, mild, severe and diabetes with complications. Most of the text is devoted to treatment, diet in the mild form, insulin for the severe type and emergency treatment for the acute, complicated form.

Physicians' Handbook. By Marcus A. Krupp, M.D., assistant clinical professor of medicine, Stanford University School of Medicine, and director of clinical pathology, Veterans Administration Hospital, San Francisco; Norman J. Sweet, M.D., assistant professor of medicine, University of California School of Medicine, San Francisco; Ernest Jawetz, Ph.D., M.D., associate professor of bacteriology and lecturer in medicine and pediatrics, University of California School of Medicine, San Francisco; and Charles D. Armstrong, M.D., clinical instructor in medicine, Stanford University School of Medicine. Sixth edition. 12°, cloth, 380 pp., with illustrations. Palo Alto, California: University Medical Publishers, 1950. $2.50.

This pocket-size handbook was first published in 1941 and last published in 1948. The text has been thoroughly revised for this edition, and some sections have been expanded. The small book, intended for students and physicians, summarizes briefly and clearly procedures and factual data needed for everyday use. The publishing is good except for the printing of valuable tables on the inside covers of the binding.

NOTICES

ANNOUNCEMENTS

Dr. Henry I. Shahon announces the removal of his office to 199 Bay State Road, Boston, for the practice of allergy.

NEW ENGLAND HOSPITAL

The monthly clinical conference and meeting of the staff of the New England Hospital will be held in the conference room of the hospital on Thursday, June 7, at 7:15 p.m. Dr. Bianca R. Lia will speak on the subject "Uterotubography — Its Role in Sterility."

AMERICAN SOCIETY OF MEDICAL TECHNOLOGISTS

The Massachusetts Association of Medical Technologists will be host to the nineteenth annual convention of the American Society of Medical Technologists, which will be held at the New Ocean House, Swampscott, on June 24–28.

REGULAR CORPS EXAMINATION FOR MEDICAL OFFICERS IN UNITED STATES PUBLIC HEALTH SERVICE

A competitive examination for appointment of medical officers in the Regular Corps of the United States Public Health Service will be held on September 4, 5 and 6, 1951, at a number of points throughout the United States. Applications must be received no later than August 6, 1951.

Application forms and additional information may be obtained from the Surgeon General, United States Public Health Service, Federal Security Agency, Washington 25, D. C. (Attention: Division of Commissioned Officers.)

(*Notices concluded on page xvii*)